

Health care reform:
Redefining biopharma
innovation



Executive summary

Health care reform encompasses legislation that has been signed in the recent past related to the access and delivery of healthcare, notably the Affordable Care Act (ACA) passed in 2010, as well as broader, nonreversible trends in the market. Reform culminates into a heightened focus on reducing cost while increasing the quality of care, which will likely force a new definition of innovation to emerge for biopharma. Historically, biopharma manufacturers and regulators have treated new molecular entity (NME) approvals as “innovative.” However, new demands from health plans and health care providers to improve the quality of care without increasing overall health care cost will increase the demand for products that demonstrate improvements in health outcomes over existing treatments. Innovation, in this new context, will be defined as:

Any combination of activities or technologies that breaks existing performance tradeoffs of therapeutic efficacy and tolerability to attain improved health outcomes in a manner that expands the realm of the possible.

While the number of new product approvals has seen a moderate upward trend in recent years, when this emerging definition of innovation is applied to these approvals, Deloitte analysis reveals less than 10 truly innovative approvals in each of the last 5 years.

This suggests that the majority of existing R&D strategies have not been focused on meeting this definition of innovation.

A shift in focus to this emerging definition of innovation will be challenged by uncertainty around returns on R&D investment, increasing scientific and regulatory risk, and new constraints on R&D funding created by reform challenges.

- **Returns on R&D Investment:** New care delivery and payment models aimed at linking the cost and quality of care will likely increase health plans and health care provider scrutiny around product utilization decisions, putting product revenues at risk.
- **Probability of Success (POS):** The Probability of Success of products getting to market that meet the emerging definition of innovation will likely decline, due to increasing Regulatory risk as the FDA considers more stringent review processes, and increasing scientific risk as companies leave crowded therapeutic areas.
- **R&D Funding:** Declining revenues accelerated by reform and increasing uncertainty around future returns are expected to make investment in R&D unattractive in the reform environment for both biopharma companies as well as venture capital.

In this new environment, organizations should refocus innovation engines so that portfolio investments are made on products that are likely to meet the emerging definition of innovation.

Reform will indirectly impact biopharma through changing stakeholder relationships

The ACA will have far-reaching consequences across the US health care industry. Yet as much as it has captured national attention, the ACA is only one of the recent, galvanizing element of a more expansive transformation of the industry driven by other state and federal reforms and, perhaps more significantly, by broader trends in the marketplace.

For many life sciences companies, health reform brings direct impacts in the form of industry taxes, rebates, comparative effectiveness data, fines and transparency requirements. However, indirect impacts related to the changing nature of their relationships to other stakeholders and the choice and consumption of their products could demonstrate an even greater catalyst for transformation. This transformation will likely increase hurdles and place new constraints on innovation.

Direct impacts: Increased access resulting from the ACA is expected to increase the volume of drug use, resulting in approximately \$26B in additional revenue over 10 years.¹ However, the Medicaid drug rebates called for by the ACA, the part D “donut hole” relief, and increase in the industry fee (levied as a percentage of profit on manufacturers) will counterbalance this increase and result in a net reduction of revenues for biopharma companies. Beyond taxes and rebates, there will be a need to invest in new capabilities that address the growing focus on and future requirements for comparative effectiveness (CE) data.

Indirect impacts: Beyond direct impacts, the biopharma industry will feel a bigger indirect impact as relationships with stakeholders evolve. The likely consolidation in the health insurance industry will impact how biopharma companies develop relationships, provide services, and focus on value. Secondly, as health care provider organizations exert greater influence over physician preferences, life science companies will likely have to shift their basic selling relationship from individual physicians to a broader set of stakeholders. Lastly, health consumers will likely become more invested in health care decisions, including those involving drugs.

Reform and the shifting power within the industry are also spurring pervasive cross-stakeholder trends that will likely have profound repercussions for innovation in life sciences. Health plan/ health care provider consolidation and integration will increase the complexity of product utilization decisions in an effort to reduce cost and improve quality of care at the same time. As an example, increasing health care provider accountability for the cost of care resulting from new care delivery (e.g., accountable care organizations) and payment models (e.g., value-based care) will result in standardization of treatment decisions based on evidence as well as cost. These cross-stakeholder dynamics will create a new standard for products that will be deemed as innovative.

Increased emphasis on quality of care under reform will redefine innovation in biopharma

While there is no standard definition of innovation in the biopharma industry, innovation has historically been accepted to be new molecular entity (NME) or priority review drugs² that receive regulatory approval from the Food and Drug Administration (FDA).

This definition casts a relatively wide net for what products are considered to be innovative. For example, new products treating a specific disease with the same mechanism of action (MOA) as an existing treatment alternative are considered to be innovative. While these drugs may expand the basis of competition within a drug class, they do not necessarily represent meaningful improvement against health outcomes, which, for the purposes of this analysis, are defined as changes in health status measured by disease-specific indicators (e.g., LDL for hypercholesterolemia) for the treatment of a specific disease. Similarly, products that improve convenience or adherence through new formulations or different delivery mechanisms have historically been considered as innovative. These products may provide value for patients, but may not be associated with improved health outcomes. Until now, there has been no differentiation among these types of innovations and relative value in terms of improvements in health outcomes.

Health plans and providers are expected to place greater value on innovations that drive significant improvements in outcomes, challenging this existing definition of innovation. This shift in the definition of innovation will be driven by reform trends such as health care provider consolidation, new care delivery and payment models, restrictive formulary design, and the increasing availability of health information. Health care provider consolidation and new care delivery models (e.g., accountable care) will result in increased standardization of care, formularies designed based on evidence, and more restrictive prescribing. At the same time, new payment models (e.g., value-based purchasing) will increase the demand for demonstrated improvements in health outcomes. As health plans look for ways to cut rising health care costs, they will be reluctant to provide formulary coverage for expensive products without substantial data proving differentiation. The establishment of Patient-Centered Outcomes Research Institute (PCORI) formalizes comparative effectiveness research and will make this data available to both health plans and health care providers to influence decision making. There will be a shift in the market to cover and utilize only those products that can demonstrate clinical differentiation.

FDA definitions

New molecular entity²: The designated therapeutic moiety in a dosage form that has not been approved for marketing in the United States (also referred to as a new chemical entity or new drug substance). It may be a complex, simple ester, or salt of a previously approved Active Pharmaceutical Ingredient.

Priority review: Preliminary estimates indicate that the drug product, if approved, has the potential to provide, in the treatment, prevention, or diagnosis of a disease, one of the following: (1) safe and effective therapy where no satisfactory alternative therapy exists; or (2) a significant improvement compared to marketed products (approved, if approval is required), including nondrug products or therapies. Significant improvement is illustrated by the following examples: (1) evidence of increased effectiveness in treatment, prevention, or diagnosis of disease; (2) elimination or substantial reduction of a treatment-limiting drug reaction; (3) documented enhancement of patient compliance; or (4) evidence of safety and effectiveness in a new subpopulation.

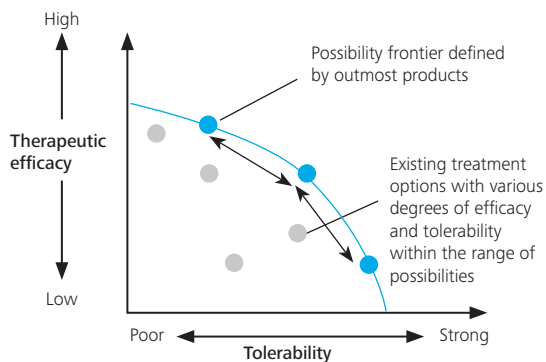
As a result of the new pressures from stakeholders, the perception of innovation is likely to start to take on a more refined meaning within the context of Health care reform. Specifically, innovation, in the context of FDA approved products, will be defined in this paper as:

Any combination of activities or technologies that breaks existing performance tradeoffs of therapeutic efficacy and tolerability to attain improved health outcomes in a manner that expands the realm of the possible.

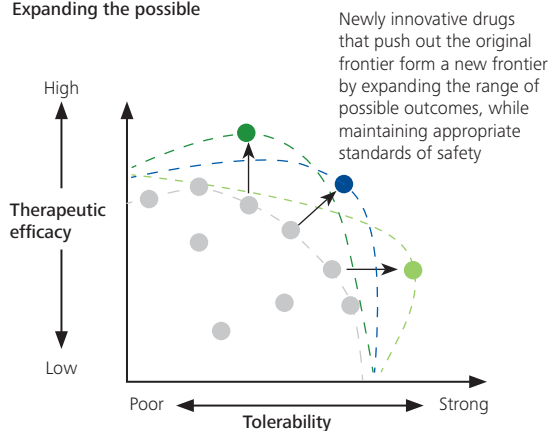
The tradeoffs of therapeutic efficacy and tolerability are important determinants of health outcomes. Therapeutic efficacy is defined as the measure of a molecule’s capacity to elicit a desired therapeutic effect, which results in an improvement in a disease-specific indicator for the disease that molecule is aiming to treat. Tolerability is defined as the measure of a molecule’s adverse properties manifested in patients who receive the medication at therapeutic doses. Breaking tradeoffs associated with therapeutic efficacy and tolerability as compared to existing treatments represents a change to the possibility frontier, or the range of possible treatment outcomes within a particular disease area given the efficacy and tolerability profiles of existing treatment options available (Figure 1). Breaking the possibility frontier represents an innovation in the treatment of a particular disease.

Figure 1. Innovation in biopharma³

Breaking tradeoffs



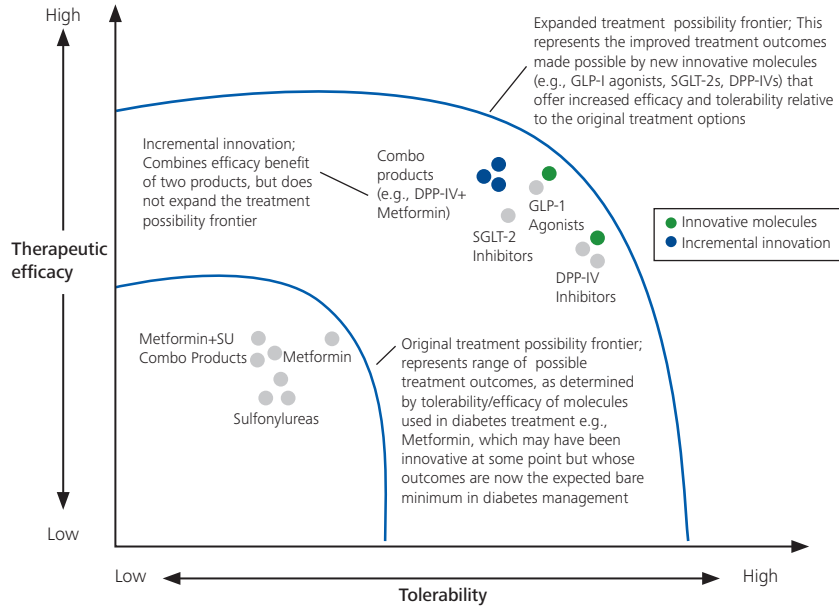
Expanding the possible



The first compound in a molecule class to break the therapeutic possibility frontier, under the definition of innovation outlined in this paper, is considered innovative. The subsequent molecules launched within a class that don't further break the possibility frontier, however, in this context, are not considered innovative (Figure 2). Similarly, while new indications create marketing approval for existing drugs to expand into adjacent disease areas or populations, they may not expand the realm of the possible, so these approvals are not considered to be innovative. In addition, new formulations and combination therapies may create benefits in terms of convenience or adherence, but if they do not significantly impact outcomes or break the possibility frontier, they are

not considered innovative under our definition. For the purposes of this analysis, these approvals are defined as incremental innovation: beneficial improvements in the delivery mechanism, dosage form or combination of an existing molecule(s) that do not expand the therapeutic possibility frontier. While these types of innovations may create value in the market from an adherence or convenience perspective, they will only be adopted in the reform environment with data that proves that they break the possibility frontier. The success of future innovation is dependent on the ability to break the possibility frontier and demonstrate differentiated value compared to current standards of care.

Figure 2. Innovation explored: Innovation in diabetes treatment (Illustrative)⁴



Price will serve as an important third dimension in the adoption of innovation

New demands for quality of care will raise the bar for products that are considered to be innovative, but additional considerations around the impact to overall health care costs will play into decisions around product utilization. Health plan and health care provider willingness to pay for new products will be determined by the additional value provided, defined as improvements in performance tradeoffs, as compared to lower cost treatment alternatives. Facing increasing pressures to decrease the cost of care, health plan and health care providers who do not believe the incremental value of a product justifies the additional cost, will not cover or utilize these products.

In fact, stakeholders are already making product utilization decisions based on this new context. Over the past few years, a number of specialty products, which may have been considered innovative, did not provide enough incremental benefit to command high price tags.⁵ Health plans and health care providers both led the charge in making this claim, either through health economics assessments or clinical experience. As a result, these products faced several challenges upon launch, and ultimately had to adjust their marketing approaches as well as decrease their forecasts.

Health economic considerations will become increasingly important for both health plans and health care providers when making product utilization decisions. Governments have already been using these types of assessments, with a prominent example being the National Institute for Health and Clinical Excellence (NICE) in the UK. NICE uses a measure called the quality-adjusted life year (QALY) to compare the economic value of drugs against each other, and drugs above a certain threshold typically do not receive national reimbursement. While the Centers for Medicare and Medicaid Services (CMS) must cover all medical products that are “reasonable and necessary” regardless of cost, they may require additional evidence to substantiate that expensive products are in fact “necessary.” In addition, private sector health plans do not have the same limitations and are expected to increasingly incorporate economic arguments into coverage decisions.⁵

With the increasing availability of real world data, enabled by the implementation of Electronic Health Records and establishment of PCORI, health plans and health care providers will be conducting their own economic assessments. For innovative products to be received positively in the market, biopharma organizations should consider embedding these types of analyses early in the development process to demonstrate sufficient cost benefit.

Recent approvals suggest biopharma strategies have not been focused on the emerging definition of innovation

Deloitte reviewed NDA approvals over the past five years to determine which ones fit the emerging definition of innovation. Our analysis suggests that the majority of recent approvals would not be considered innovative in the reform environment.⁴ Given this context, biopharma companies will need to refocus innovation engines so that future products are likely to achieve a return on investment in the evolving marketplace.

Historical analysis

Deloitte assessed the level of recent innovation within the biopharma industry using the segmentation described on the right. While the FDA cited 35 innovative approvals in 2011, defined as NMEs and priority reviews,⁶ under our definition of innovation, there were only 7 innovative approvals (Figure 3).⁴ The majority of the 35 innovative approvals in 2011 were NMEs using an already established MOA, or “me-too” drugs. Expanding this analysis over 2007-2011 (Figure 4), there have been less than ten innovative drug launches per year. Similar to 2011, the majority of FDA approvals within the past five years have been “me-too” drugs. A deeper look at therapeutic areas (TAs) reveals that Metabolism, Cardiology, and Infectious Diseases are associated with the highest number of “me-too” launches. While these TAs treat broad patient populations, the lack of innovation in these TAs suggests that they have now become crowded, with little room for future innovation capable of breaking the possibility frontier.

Deloitte analyzed innovative approvals and found that innovation, by our definition, over the past several years tends to fall into three TAs: Orphan Diseases, Neuroscience, and Oncology (Figure 5). TAs with a greater percent of innovative approvals (within the TA) than the total percent of innovative approvals with the year, across two or more of the years from 2009-2011 is defined as being associated with innovation.

Products in the TAs associated with innovation treat complex diseases where little is known about the molecular cause of disease and there is high unmet need. Additionally, within these TAs, products generally treat smaller, more targeted populations. Future innovation is likely to come from these TAs.

FDA drug approval categorization

Potential Innovation	New molecular entity (NME)
Incremental Innovation	New active ingredient
	New dosage form
	New combination
	New formulation or new manufacturer
	New indication
	Drug already marketed without an approved NDA
	OTC switch
	New indication submitted as distinct NDA

Categorization methodology

The nine FDA NDA drug approval categorizations were segmented in order to determine how many approvals met the emerging definition of innovation.

The majority of innovation occurs within drugs categorized as NMEs. This category can be further broken down into subcategorizations to identify which products meet the emerging definition:

Not-Innovative

- “Me-too” products, molecules that exert their effect via an already established mechanism of action

Innovative

- Drugs that act by a new mechanism of action
- Drugs that treat diseases where there have historically been limited treatment options such as orphan diseases

Other categories of approvals are considered to be incremental innovations because they do not significantly impact outcomes or break the possibility frontier. Each of the categories in light green above are considered incremental innovations for the purpose of this analysis.

Figure 3. 2011 NDA approval analysis⁴

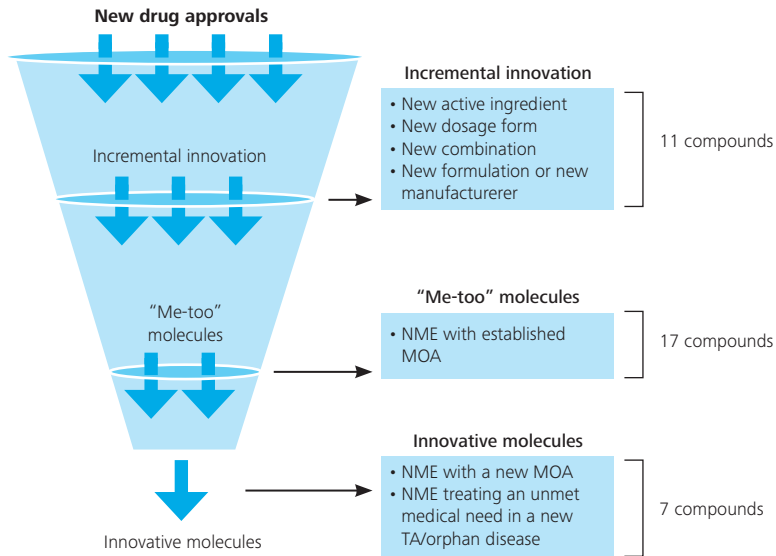
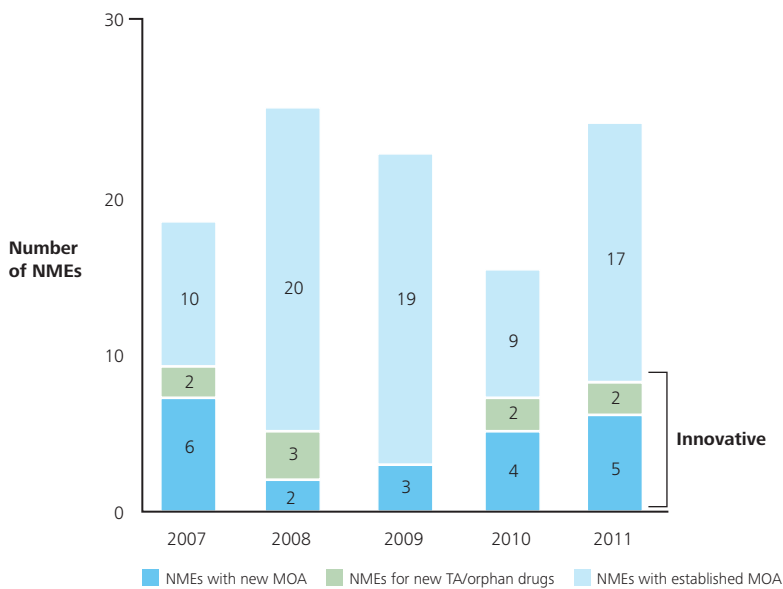


Figure 5. Innovation by TA^{4, 7}

Therapeutic Area	% of "innovative" launches/year		
	2009	2010	2011
Cardiology	0%	0%	0%
Gastroenterology	0%	0%	0%
Genitourinary	0%	0%	0%
Hematology	0%	0%	0%
Respiratory	0%	0%	0%
Infectious Disease	0%	50%	20%
Immunology & Inflammation	0%	0%	20%
Orphan Disease (Metabolism)	25%	67%	0%
Neuroscience	0%	67%	50%
Oncology	50%	50%	75%
Total % innovative of molecules	14%	40%	29%

Figure 4. Approvals by molecule type⁴



Reevaluating the current portfolio

Current R&D investments may not realize acceptable returns, due to shifting market conditions and a higher bar for meeting the requirements for innovation. Return on R&D investment is currently declining as the average value of forecasted sales of new products in late stage development is declining. Biopharma companies should redesign innovation engines in order to realize sufficient ROI on future investments.

A Deloitte and Thomson Reuters review found that the industry's IRR from R&D has been dropping steadily over the past few years (10.5% in 2010 to 7.7% in 2011, and to 7.2% in 2012). While the number of approvals in 2012 exceeded those of 2011, the total sales value of approvals (over 21 years) has declined from \$309B to \$211B. Furthermore, the total forecast value of late stage compounds in development has declined from \$1,369B in 2010 to \$1,049B in 2012.⁸ There are a number of factors aside from reform that could be contributing to this including economic factors and productivity challenges; however, the data suggests that a shift in innovation models is required.

Biopharma companies should ask questions to test how innovative their portfolio is in the context of the emerging definition of innovation, including:

- Is our R&D investment heavily concentrated in therapeutic areas where there is little room to break the possibility frontier? Are we investing in therapeutic areas where there is unmet need?
- Do drugs in our current pipeline meet this definition of innovation and break the current status quo in terms of therapeutic efficacy and tolerability?
- Will our current products be able to meet forecast expectations given new market demands?

Consequently, biopharma companies should reevaluate portfolio strategies to take steps to develop candidates that break therapeutic efficacy and tolerability performance tradeoffs. Refocusing investments will need to be done in the context of existing productivity challenges as well as additional challenges placed on innovation as a result of reform impacts.

Challenges to successful innovation in the reform environment

Reform will create new challenges for biopharma companies to navigate as they work to redefine innovation engines. These challenges include increased uncertainty around returns on R&D investment, increased scientific and regulatory risk, and new constraints on R&D funding.

Returns on R&D investment

As a result of reform, health plans and health care providers will begin to take an even more rigorous approach to formulary and treatment decisions. This shift will be driven by the increased availability of data, as well as the increasing prevalence of cost containment strategies that link payments (physician and product) to outcomes. Now, utilization decisions for new products will be made based on where that product sits on the possibility frontier. Market adoption of new products will require evidence that demonstrates that these products are breaking the possibility frontier, and providing a benefit in terms of improved outcomes. The demand for this kind of evidence increases the hurdles to realize a return on R&D investment. Without evidence that demonstrates a product's ability to break the possibility frontier, returns on R&D investment will continue to decline.

Comparative effectiveness: Formulary decisions will be made on the basis of an increasing volume of comparative effectiveness data, partly accelerated by the establishment of the PCORI. More restrictive markets such as the UK and Germany have already embedded this type of decision making into designing national formularies. Many products that would traditionally be considered as innovative are not available in these markets. In fact, Deloitte analysis of the 340 top selling drugs in the US during 2011, revealed that nine out of 96 specialty products are not on formulary in both the UK and Germany.⁴ If the US follows suit, restricted access to these types of products may put downward pressure on revenues.

Value-based pricing risk sharing examples

Risk sharing agreements will become increasingly common if the evidence that a product breaks the possibility frontier is not compelling enough.

Oncology:

NICE in the UK concluded that Velcade was too expensive relative to its estimated benefit to the population. In response, J&J offered to forgo charges for patients who did not have an adequate medication response²⁰

Neuroscience:

The Swedish Institute for Health Economics conducted a case study of Duodopa in advanced Parkinson's disease, which concluded that: (1) stakeholders benefited from analysis of real world (postmarket) data (in addition to pre-launch, trial-based data); and (2) conditional coverage allowed for effective risk sharing and sufficient access to pharmaceuticals by consumers²

Value-based pricing: Health plans are continuing to expand strategies that include elements of risk sharing as a means to control prescription drug costs. Value-based pricing agreements will provide greater transparency into the contribution of the prescription to the value and outcomes provided to the patient. This shift will increase the risk taken on by manufacturers, as well as uncertainty around returns.

Novel care delivery approaches: With the advent of value-based care delivery models (e.g., Accountable Care Organizations, Medical Homes), physicians will be incentivized to improve outcomes at lower costs. Physician groups will increase scrutiny of new products to determine if relative improvements in outcomes warrant additional costs. In addition, consolidation across the health care provider sector will result in a shift of decisionmaking away from individual physicians towards physician groups, who will design standardized protocols based on evidence. Revenues for products that are not selected to be on those standardized protocols will suffer.

Probability of success

Pursuing innovation in the reform environment will be challenging due to increasing risk and declining POS. POS has traditionally been thought of as the combination of regulatory and scientific risk on the path to approval. Regulatory uncertainty is expected to increase as a push for greater assurance of patient safety has resulted in intensified FDA scrutiny on new drug and biologic applications. In addition, innovating in diseases where the underlying science is complex will create new technical challenges that will also decrease POS.

An increase in public demand for higher safety and efficacy standards has resulted in an increase in regulatory pressures for industry over the past several years. This has been triggered by a series of postmarketing safety events that have resulted in label changes, black box warnings, or product recalls. As a result, the FDA has increased pre-approval safety requirements including requests for more clinical trial data, higher number of patients in clinical trials, and more detailed trial analysis. The already lengthy and expensive process of obtaining regulatory approvals has become more challenging, and the chances of rejection have increased.⁹

Case example

Increased scrutiny led to rejection of Xarelto for treatment of ACS

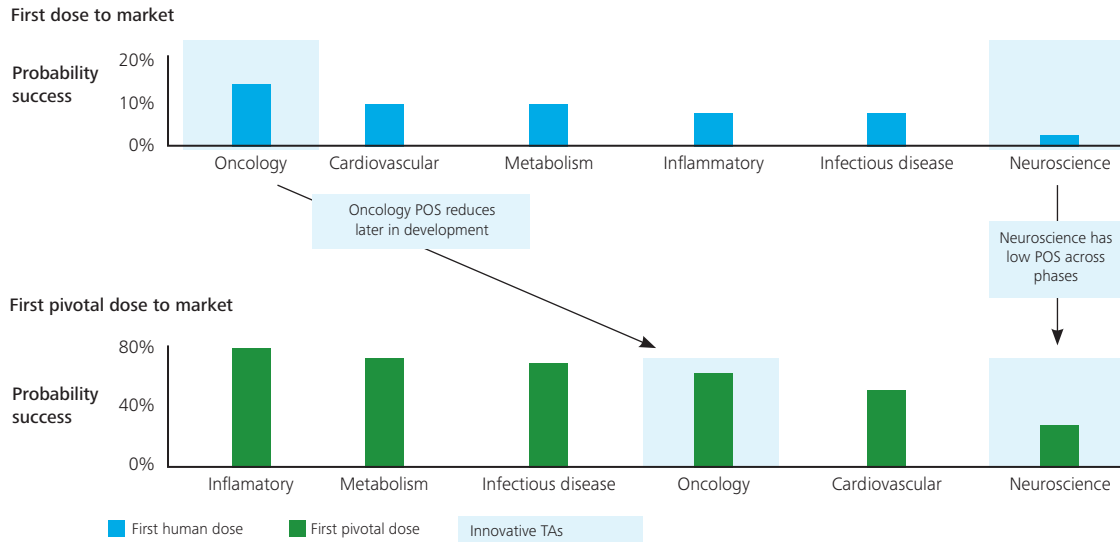
Janssen, a division of Johnson & Johnson, sought to expand the uses of its blood thinner, Xarelto, to include patients with a common heart condition known as acute coronary syndrome (ACS). However, the FDA rejected the new use for the drug. The FDA panel cited concerns about bleeding risk and missing data from the pivotal ATLAS trial of the drug.²²

Though Xarelto was found to reduce the risk of death or stroke by 15% among patients recently hospitalized for ACS, FDA was concerned that the researchers had incomplete outcomes data on 12% of the study participants.²³

In addition to current challenges, other potential downstream changes to the FDA process may further complicate the approval process. Specifically, the FDA has recently reexpressed its commitment to Advancing Regulatory Science, which includes initiatives to “continue and expand patient centered outcomes research by compiling datasets converted to standardized format across critical classes of drugs.” With these new capabilities, there is speculation that the FDA may include comparative risk/benefit analysis in the approval process, and grant market access based on comparative clinical value rather than data on independent outcomes.¹⁰ In addition, there may be a shift towards conditional registration with lifecycle regulation to reduce safety risk associated with exposure to broader populations.

Beyond regulatory challenges, therapeutic areas associated with recent innovation (Oncology, Neuroscience) have lower POS than those less likely to be associated with innovation (Cardiology, Metabolism, Infectious Disease), as seen in Figure 6 below. These innovative therapeutic areas face greater scientific challenges, increasing the development risk. In order to break the performance tradeoffs of therapeutic efficacy and tolerability, organizations will likely need to expand investments in these complex disease areas, where scientific risk is greater.

Figure 6. POS at key milestones¹¹



R&D funding

Reform pressures negatively compress revenues across the industry, resulting in cuts to internal R&D funding. At the same time, venture capital investment will continue to decline as a result of increasing risk associated with biopharma investments.

Declining emphasis on R&D: After years of increasing R&D budgets, large biopharma organizations are now cutting internal R&D funding in the face of decreasing revenues and increasing shareholder expectations. Total R&D budget for the 10 largest biopharma companies increased from \$59B in 2008 to \$71 B in 2010, but has since started to decline.¹¹ As the costs associated with drug approval increase and associated revenues decrease, shareholders place increasing scrutiny on additional R&D investments. According to an analyst quoted in the Burrill Report, investing in R&D is no longer seen as a strength, instead “spending more doesn’t mean getting anything out”.¹²

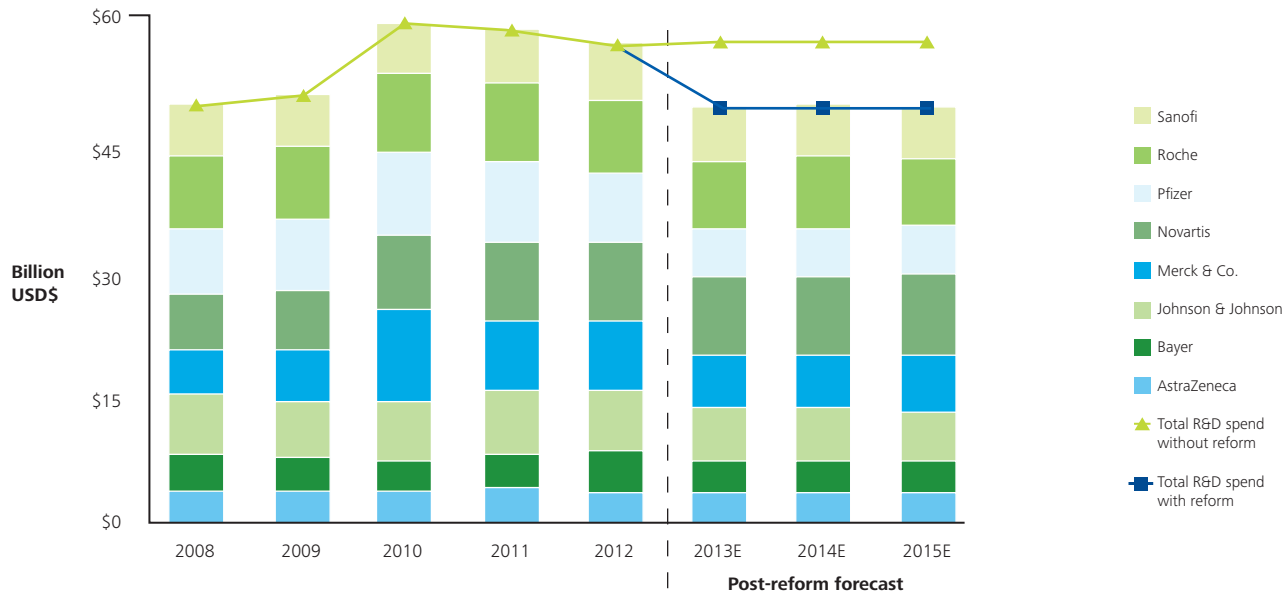
Formulary pressures: Revenues and the availability of funds to support R&D internally will be further compressed due to formulary pressures exacerbated by reform. Increasing formulary pressures are expected to

decrease industry revenues by 13.7% in 2015.¹³ As a result, R&D budgets, typically allocated as a percentage of revenues, will decline in conjunction.

The impact of the increase in formulary pressures, on top of the current reductions in R&D budget, is forecasted to push R&D budget below 2009 levels through 2015 (Figure 7).

Venture capital investment: Overall venture capital investment in the life science industry is decreasing, as evidenced by the decline in the total value of the investments since 2007 (Figure 8). Increased FDA scrutiny and regulatory hurdles for approval, scientific risk, and reimbursement pressure along with higher costs for drug development all contribute to the decline in life sciences investment. At the same time, the downward trend is further complicated by current economic pressures. As reform continues to unfold, this trend is expected to continue as the risk and hurdles associated with drug development continue to increase. In fact, a recent survey indicated that almost 40% of Life Sciences VC firms intend to invest less in the next 3 years, citing the main cause as the cost, time and unpredictability of the regulatory landscape.¹⁵

Figure 7. R&D investment pre- and post-reform^{13, 14}



In addition, there are shifts in the average size and the type of investments the VC community is making in biotech and pharma (Figure 9). The average number of investors per deal has been declining since 2007, while the average size of investment has been increasing. This trend suggests that investors are making greater, more focused bets on areas where they have greater confidence. In addition, a greater proportion of investments is shifting away early stages of development (discovery and preclinical) towards later stages of development (Phase I-III). Specifically, between 2010 and 2011, there was a 5% reduction in investment in discovery and preclinical phases, but a 4% increase in investment in the development phases.¹⁶ As a candidate progresses through development, its POS increases, development risk goes down, and investment becomes more attractive. Overall, VCs seem to be shifting focus to investments associated with less development risk.

Venture capital investments are also shifting away from TAs associated with innovation, further diminishing the ability of private investment to drive future innovation (Figure 10). Overall investment in TAs associated with innovation is higher than in those TAs associated with less innovation; however, recent trends show that investments in these TAs have been steadily decreasing between 2009 and 2011.¹⁷ Investments in innovative TAs are likely associated with greater development risk, and a shift in investment to less innovative TAs might indicate a decreased willingness by VCs to place bets on these complex TAs. The basis of disease is better understood and more predictable in TAs associated with less recent innovation; making investments in these areas more attractive.

Figure 8. Venture capital investment in biotech and pharma (2007-2011)¹⁷

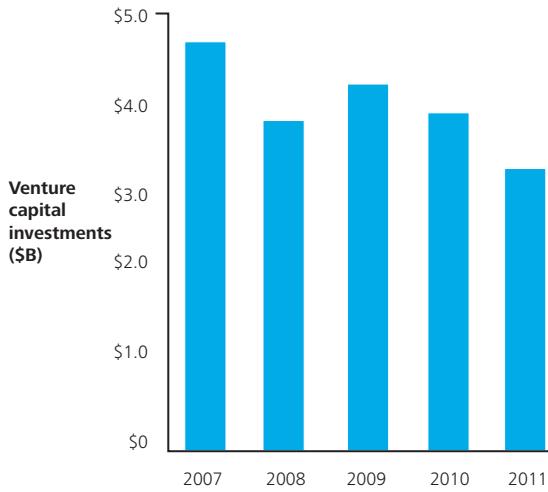
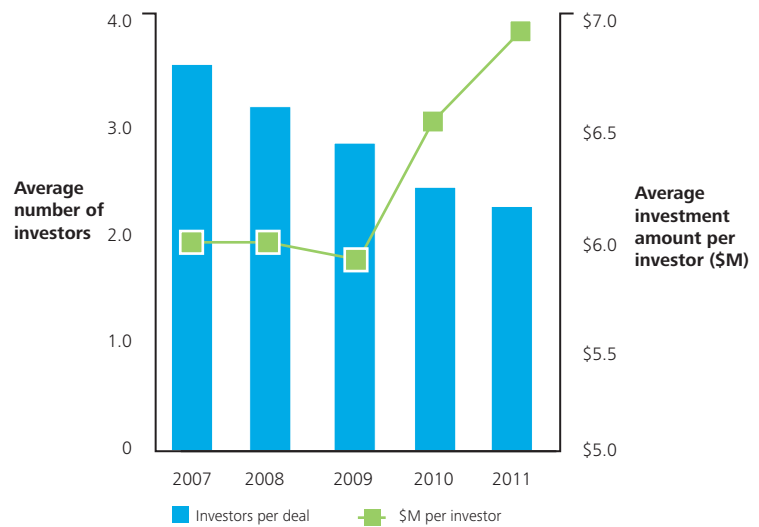


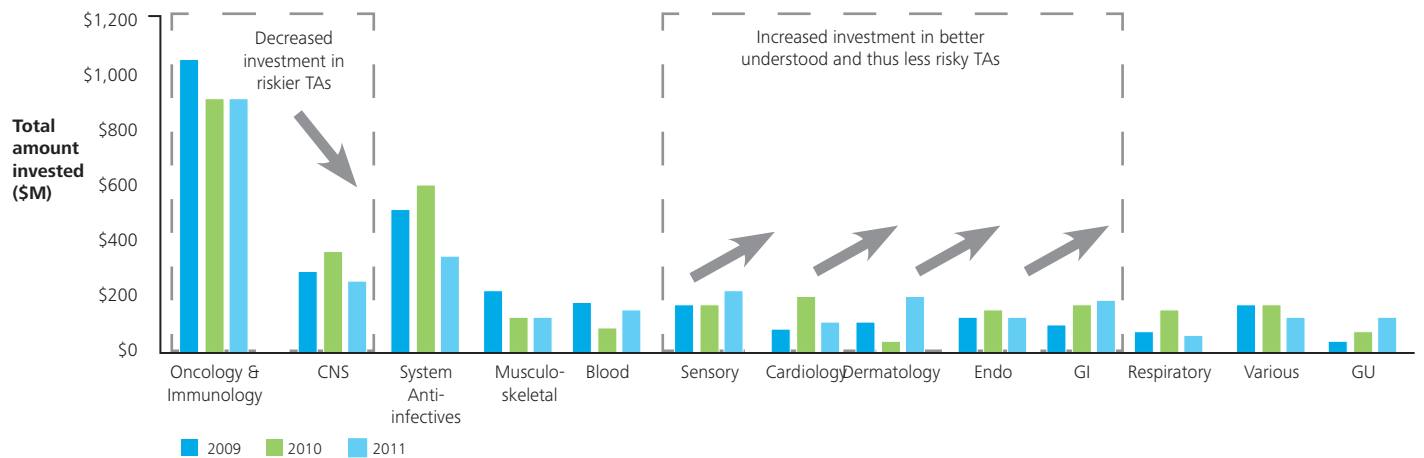
Figure 9. Number of investors per deal vs. average investment amount per investor (2007-2011)¹⁷



The shift towards investing in demonstrated, lower risk candidates suggests that there will be less funding for development candidates aligned with the emerging definition of innovation under reform. This trend will decrease the supply of innovation at a time when biopharma organizations are increasingly looking externally to source innovative assets. The average percent of a company's pipeline in-licensed in the top 10 biopharma

companies has risen from 33% to 38% between 2009 and 2011.¹⁸ Deals in neurology and cancer have the highest deal value as these are associated with the highest levels of innovation, and therefore provide the highest value.¹⁹ However, as VC investments drop in these innovative TAs, biopharma companies will have fewer VC backed companies across these areas to in-license from, thus further depleting sources for innovation.

Figure 10. Total VC investment by TA 2009-2011^{17, 4}



Driving innovation forward in the new environment

A new definition of innovation reinforced by stakeholders, coupled with new development challenges, will increase hurdles to realize a return on investment in R&D as reform continues to unfold. Successful future innovation will depend on the ability to appropriately focus R&D investments on products that break the possibility frontier and generate a strong body of evidence that demonstrates significantly improved outcomes. With R&D funding on the decline, a focused and well-defined portfolio strategy will be critical. Investments should be made in areas where there is high unmet medical need, and greater opportunity to break the possibility frontier. However, scientific challenges will remain in these areas, and organizations should think strategically about development approaches, designing experiments to elucidate where a candidate sits on the possibility frontier. Furthermore, the scope of development efforts will expand beyond demonstration of clinical benefit to include demonstration of comparative and cost benefit. Organizations that do not effectively adapt to the new environment and refocus innovation engines now may continue to see declines on returns on R&D investments, and may rethink investing in Research all together.

Reshaping the portfolio. Health plans and health care providers are not likely to utilize a product that does not break the possibility frontier, especially if alternative treatments are available at a lower cost. Organizations should take a hard look at current portfolio investments and assess competitive threats under a new lens, linking relative value in terms of health outcomes with cost. Specifically, organizations should ask themselves:

- Do our forecasts for candidates in development account for new pressures in the market? What are realistic returns on products in development that use an established MOA, or treat diseases with multiple treatment alternatives?
- How do our pipeline products compare against alternative treatment options?
- How should we prioritize the portfolio under the context of this new definition of innovation?

- Should we focus R&D investments on a broad set of TAs or focus on a select group of disease areas where the unmet need is high, and there is greater likelihood to break the possibility frontier?

Accessing innovation. As the VC environment shifts funding away from TAs associated with greater innovation, organizations should consider whether or not their internal research engines will be able to produce candidates that meet new portfolio goals. Organizations should consider:

- Where will private investors place bets in biopharma? Will there be enough external candidates to pursue to meet inorganic growth (licensing/acquisition) targets?
- What types of strategic external investments and partnerships are required to fill gaps?

Redesigning research. Future portfolios are likely to be focused on areas with complex science and low POS. Organizations should rethink traditional research programs and design experiments that will generate critical data early in development. Early experiments should be designed to understand where a product may fall on the possibility frontier, decreasing scientific uncertainty associated with the asset. Organizations should consider:

- How can we design early experiments to reduce the scientific uncertainty associated with an asset?
- How can we maximize investments in early in development to focus on experiments that reduce scientific uncertainty?
- How can we redesign decision-making processes so that only those compounds that are likely to push the frontier make it through into development?

Ten Types of Innovation®

Through empirical study and over 30 years of research and practical application, Doblin, the innovation practice of Monitor Deloitte, developed one of the world's most recognized frameworks in the field of innovation. They discovered that leading innovators, and truly breakthrough innovations, go beyond just product innovation. Their analysis uncovered that there are Ten Types of Innovation® which are rich sources for new value. Building on that discovery, they saw an enduring result that consistently effective innovators have adopted a mentality that breakthroughs occur by deploying multiple types of innovation in concert.



Source: Doblin.com/TenTypes

For BioPharma the challenge is even more acute as stakeholders re-set product expectations. The trap is to approach this challenge with a lens narrowly focused on the product. Traditional levers for “better, faster, cheaper” simply will not be enough. Meeting these new expectations will demand flexing new muscles, across multiple types of innovation. Explore how you *configure*, by assessing the role of external innovation networks and new research processes early in the development process. In parallel, consider the potential of *customer experience* innovation for your important access and regulatory stakeholders could improve the communication and understanding of product value.

Moving forward in this new environment, ask yourself a few specific questions:

- Which types of innovation are you focusing on today?
- Where do you have blind spots and potential untapped opportunity?
- How can you bring multiple types of innovations to existing R&D activity?

Generating evidence. A substantial package of evidence will be required to demonstrate that an innovative product pushes the possibility frontier. Development programs will now need to be designed to generate data that substantiates products are more effective than the current standard of care, and that the incremental benefit created is sufficient to command high costs. Organizations should consider the following questions:

- What types of comparative and economic data do we need to gather to demonstrate to regulators, health plans, and health care providers that our products are pushing the possibility frontier and improving performance trade offs?
- How can we engage health plans and health care providers to understand comparative and economic requirements?
- How can we collaborate with health plans and health care providers to access real world evidence for comparative studies?

Reconsidering the operating model. The challenges ahead of the biopharma industry are not insignificant. Some organizations might find the challenges too hard to overcome, and failed investments may lead to considerations of forgoing Research altogether. The following questions should be considered:

- What are our core competencies and what value are we generating from organic Research efforts?
- Should we continue to invest heavily into Research or should we shift focus to other parts of the value chain where returns may be higher (e.g., commercialization capabilities in emerging markets)?

Glossary and endnotes

Glossary

- **Efficacy:** Refers to the measure of a molecule's capacity to elicit a desired therapeutic effect
- **Health outcomes:** changes in health status measured by disease-specific indicators (e.g., LDL for hypercholesterolemia)
- **Incremental innovation:** Refers to beneficial improvements in the delivery mechanism, dosage form or combination properties of an existing molecule(s) that do not expand the therapeutic possibility frontier
- **Innovation:** Any combination of activities or technologies that breaks existing performance tradeoffs of therapeutic efficacy and tolerability to attain improved health outcomes in a manner that expands the realm of the possible
- **Mechanism of action:** Refers to the specific biochemical interaction/means through which a drug substance produces its pharmacological effect
- **'Me-Too' molecules:** Refers to molecules that exert their effect via an already established mechanism of action irrespective of advancement in the drug preparation
- **New molecular entity:** Refers broadly to a therapeutic molecule that has previously not been approved for marketing in the US. This could be a new molecule, a complex, simple ester, or salt of a previously approved Active Pharmaceutical Ingredient
- **Possibility frontier:** The range of possible treatment outcomes within a particular disease area given the therapeutic efficacy and tolerability profiles of existing treatment options available in that disease area
- **Tolerability:** Refers to the measure of a molecule's adverse properties manifested in patient receiving the medication at therapeutic doses. It is a measure of the safety profile of the drug at therapeutic doses

Endnotes

- ¹ Deloitte Review: Moving Target Life sciences, health care reform and the new marketplace
- ² Products adjudged to potentially offer substantial treatment benefits are considered, by the FDA, under the priority review system. CDER Manual of Policies and Procedures (MaPP) 6020.3 explains the priority review policy and procedures: <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm082000.pdf>
- ³ Adapted from Michael E. Raynor "The Innovator's Manifesto." 2011
- ⁴ Deloitte Consulting LLP
- ⁵ Failure to Launch. Nature biotechnology. January 2013
- ⁶ FY11 Innovative Approvals. FDA. November 2011
- ⁷ A TA is associated with innovation when the TA has a greater % launch of innovative compounds (within the TA) than the total % innovative launch across 2 or more of the years from 2009-2011
- ⁸ Measuring the return from pharmaceutical innovation 2012: Is R&D earning its investment? Deloitte Thompson Reuters
- ⁹ Fitch: Global Pharmaceutical Approvals Moderate as Patent Cliff Peaks (2012)
- ¹⁰ In Vivo. Watchdog And Innovator: Modernizing The FDA-Industry Relationship. Nov 2012. Advancing Regulatory Science: <http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm267719.htm>
- ¹¹ Thomson Reuters. CMR International 2012 Pharmaceutical R&D Factbook. May 2012
- ¹² Burrill & Company. "Biotech 2012: Innovating in the New Austerity"
- ¹³ Deloitte analysis on financial impacts of Health Reform on Life Sciences industry; Direct impacts include: Coverage expansion, Medicaid drug Rebate program expansion, Part D "Donut hole" relief and Industry fees; Indirect impacts include: Formulary pressure and Competition from Biosimilars
- ¹⁴ Market projections based on industry and company reports; post reform forecast is based on Deloitte Analysis
- ¹⁵ NVCA Vital Signs Report
- ¹⁶ Parexel Sourcebook (Morgan Stanley Research)
- ¹⁷ EvaluatePharma US Venture Capital investment data
- ¹⁸ Parexel Sourcebook (Citeline Inc., Pharmaprojects/Pipeline); Elsevier Strategic Transactions
- ²⁰ Garber AM, McClellan MB. "Satisfaction Guaranteed – 'Payment by Results' for Biologic Agents." New England Journal of Medicine. 2007;357(16):1575–7.
- ²¹ Willis M, et al. "Reducing Uncertainty in Value-Based Pricing Using Evidence Development Agreements. The Case of Continuous Intraduodenal Infusion of Levodopa/Carbidopa (Duodopa®) in Sweden." Applied Health Economics and Health Policy. 2010;8(6):377-86.
- ²² <http://www.internalmedicineneeds.com/single-view/fda-panel-rejects-acs-indication-for-rivaroxaban/6a3d1dd620e6f06ef91230a8a3bf9301.html>
- ²³ <http://www.webmd.com/dvt/news/20120622/fda-rejects-new-use-for-blood-thinner-xarelto>

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