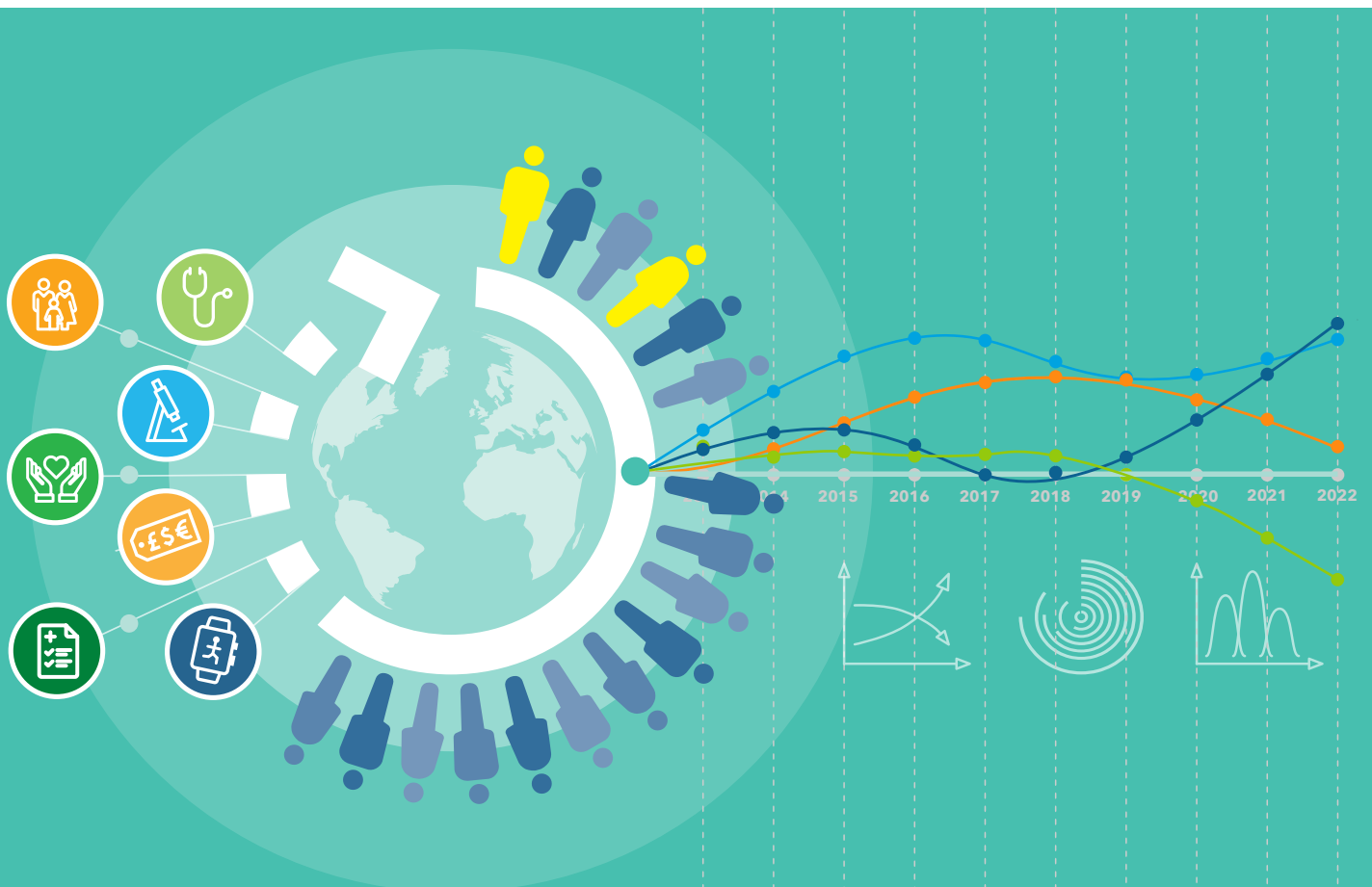


MARCH 2018

# 2018 and Beyond: Outlook and Turning Points



# Introduction

Global health is poised to meet a series of key turning points, and changes seen in 2018 will mark the key inflections that drive the outlook for the next five years and beyond. The types of medicines being developed, the way technology contributes to health and how the value of healthcare is calculated are all changing, markedly.

This report calls out ten predictions for 2018 and beyond, highlighting the background, and the implications for stakeholders, of each one.

Innovation is a key theme. Both regulators of medicines and applicants filing for approval will increasingly support clinical submissions with real-world data. A wave of cell and gene therapies is bending the definition of what constitutes a drug, both clinically, and in terms of expectations of outcomes, duration of treatment and costs. Technology itself can be a treatment, and mobile apps are newly appearing in treatment guidelines as a key feature of future care paradigms. Furthermore, mobile technology can be an enabler of telehealth communication that brings providers and patients together at substantially lower costs than traditional consultations.

In recent years, concerns about escalating medicine costs have captured significant attention. In 2018, some of the key drivers of medicine spending growth appear to be slowing spending rather than driving it upward. The causes of slowing growth are directly linked to payers' concerns about budgets and to newly emerging mechanisms to adjudicate value and thus limit the potential for out-of-control spending growth.

Overall, this report highlights impactful areas where stakeholders are using evidence and technology to solve the problems of human health. By focusing on evidence and balancing emotional issues with facts and data, we hope these articles will offer useful input to stakeholders grappling with these critical issues.

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# FDA guides use of real-world data for medicines

## BACKGROUND

As Big Data gathered in real-world healthcare settings becomes more prevalent and robust, it is increasingly being used across the entire healthcare system for evidentiary purposes or as Real-World Evidence (RWE). Both granular and timely, this data – which includes electronic health records (EHRs), claims data, disease registries, among other sources<sup>1</sup> – can shed light on the use, benefits and risks of medicines outside of clinical trials. Payers have already broadly adopted its use to guide value decisions on drug reimbursement, but only recently have clinical trial sponsors and regulatory bodies also sought to bring the value of this data to bear on the drug development process, realizing its potential to accelerate approvals and increase the robustness of the evidence generation process across a medicine’s lifecycle.

## OUTLOOK FOR 2018 AND BEYOND

In 2018, the United States Food and Drug Administration (FDA) will issue its first framework addressing the potential for RWE to accelerate the drug approval process, taking the first formal steps to expand the types of evidence trials they will accept. The 21st Century Cures Act, which became law in 2016, tasked the FDA to identify key uses of RWE to supplement medicine approvals, first as a Framework (expected December 2018), and ultimately as a Guidance (expected by December 2021).<sup>2</sup> This will clear a path for drug manufacturers to make use of RWE sources in the regulatory process. Looking to public documents authored by FDA employees and a recent Guidance document on the use of RWE for medical device approvals<sup>3</sup> the key areas that RWE is predicted to support cover both new indications for previously approved drugs and the post-approval environment (see Exhibit 1).<sup>2,4</sup>

## IMPLICATIONS

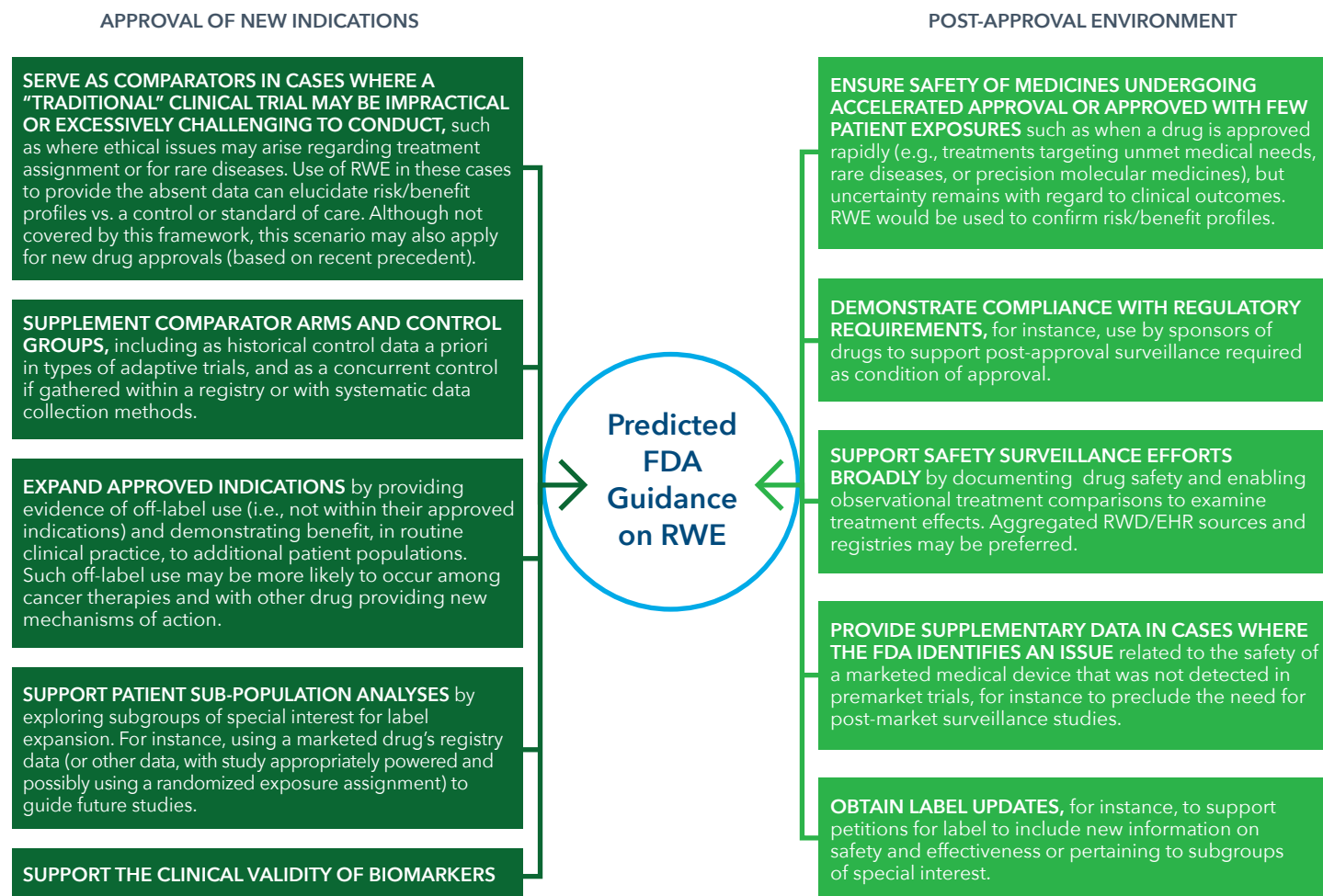
This framework, along with recent guidance on RWE use for medical devices, reflects a new willingness by

the FDA to use RWE to lighten the regulatory burden. With this shift, regulators will be both enabled and challenged to accelerate the pace of their review through new data-derived protocols, insights and approaches, and this will likely foster more collaborative approaches between life sciences companies and the FDA around trial design.

It also reflects an acceleration in the pace of change at the FDA. The framework is a first important step by the FDA to liberalize the types of trials they will accept as evidence; a shift that will extend beyond RWE use as the FDA moves to incorporate new information and technologies. In line with U.S. FDA Commissioner Gottlieb’s statements expressing support for new reliable models of evidence generation<sup>5</sup> and the 2018 FDA Strategic Policy Roadmap released in January 2018, the FDA intends to not only define a role for RWE, but also build a policy framework to “modernize approaches to clinical trial design,” support accelerated approvals and adapt to future regulatory needs.<sup>6</sup> As part of these efforts, the FDA is also likely to embrace other novel trials designs, such as pragmatic trials that test medicines in routine clinical practice settings, and adaptive trials, where trial endpoints can be changed midway through a trials based on pre-defined parameters.

The FDA’s RWE framework is likely to have significant impact on clinical trial design. By providing the first detail on the FDA’s methodological approaches to leverage real-world data (RWD) appropriately, it will help life science companies identify a range of regulatory uses for RWE in the drug and biologics regulatory process; even those beyond the scope of the framework, including the support of primary indications. Manufacturers are likely to rapidly shift their approaches to clinical development. The FDA has already signaled it will additionally accept the use of RWD for initial approvals of new drugs addressing high unmet need, setting a precedent through its approval of avelumab (Bavencio) for rare metastatic Merkel cell carcinoma, where RWD comparators were assessed as benchmarks describing the natural history of the disease.<sup>7,8</sup> A possible shift towards more routine use of RWE as comparators in trials might offer the possibility to shrink

## Exhibit 1: Real-World Evidence in Medicines Regulation: Priority Use Areas Likely to be Addressed by the FDA



Source: FDA. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Guidance for Industry and Food and Drug Administration Staff Document. Aug 2017; Sherman RE, M.D., M.P.H., et al. Real-World Evidence – What Is It and What Can It Tell Us? N Engl J Med 2016; 375:2293-2297; IQVIA Institute Analysis, Feb 2018

Notes: RWD = Real-World Data; RWE = Real-World Evidence.

control arms. For manufacturers that have seen ever-rising R&D costs and shrinking available markets for new drugs, the movement of the FDA very attractively offers the possibility of slowing the growth of R&D costs, multiplying the number of new medicines that can be developed and approved from the same spend, and speeding approvals.

For patients, the use of RWE offers the possibility of gaining access to novel medicines more rapidly, enabling the FDA to accelerate approvals while ensuring an appropriate benefit-risk balance. With the explosion of combination cancer regimens, the use of RWD by regulators could bring the examination of greater levels

of evidence for a wider variety of regimens than would otherwise be funded. In areas where off-label usage is common, it also offers to accelerate expanded use, as drugs gain a means to move from off-label to on-label with limited fuss. For payers, one mechanism to control healthcare costs has been to favor reimbursement for on-label uses. Should a large group of off-label uses rapidly become on-label, reimbursement will likely need to adjust. Payers will need to monitor these approval trends closely. If approvals are accelerated, clinical bodies will increasingly need to aggregate, review and disseminate new standards, based on this flow of real world data derived findings, and do so more rapidly and clearly than ever before.

**AREAS OF INNOVATION**

## Next Generation Biotherapeutics move toward mainstream

**BACKGROUND**

Over the past few years, a new generation of cell-based therapies, gene therapies and regenerative medicines (e.g., Next Generation Biotherapeutics) has begun to complete clinical trials and gain regulatory approval, with agencies now categorizing and granting breakthrough designations for these types of therapies.<sup>9</sup> These treatments stretch the definition of a drug – by being engineered personally for each patient, and some offer curative results with a single administration. In certain cases, these characteristics also result in an extremely high-cost per patient relative to traditional, small molecule therapies. Many of these approaches are too new to have proven outcomes, and the combination of this uncertainty with high costs is impacting the dynamics around how these medicines will be paid for and used. The wide range of mechanisms and production methods used by emerging Next Generation Biotherapeutics are shown in Exhibit 2.

**OUTLOOK FOR 2018 AND BEYOND**

In 2018, between five and eight Next Generation Biotherapeutics will be approved and launched. Over the next five years, 20% of the 40–45 New Active Substances (NAS) projected to be launched each year will come from this group of drugs. The pipeline of 142 next generation drugs in late-stage research represents just five percent of ongoing late stage research but will be more successful than other areas and will reach the market in large numbers.

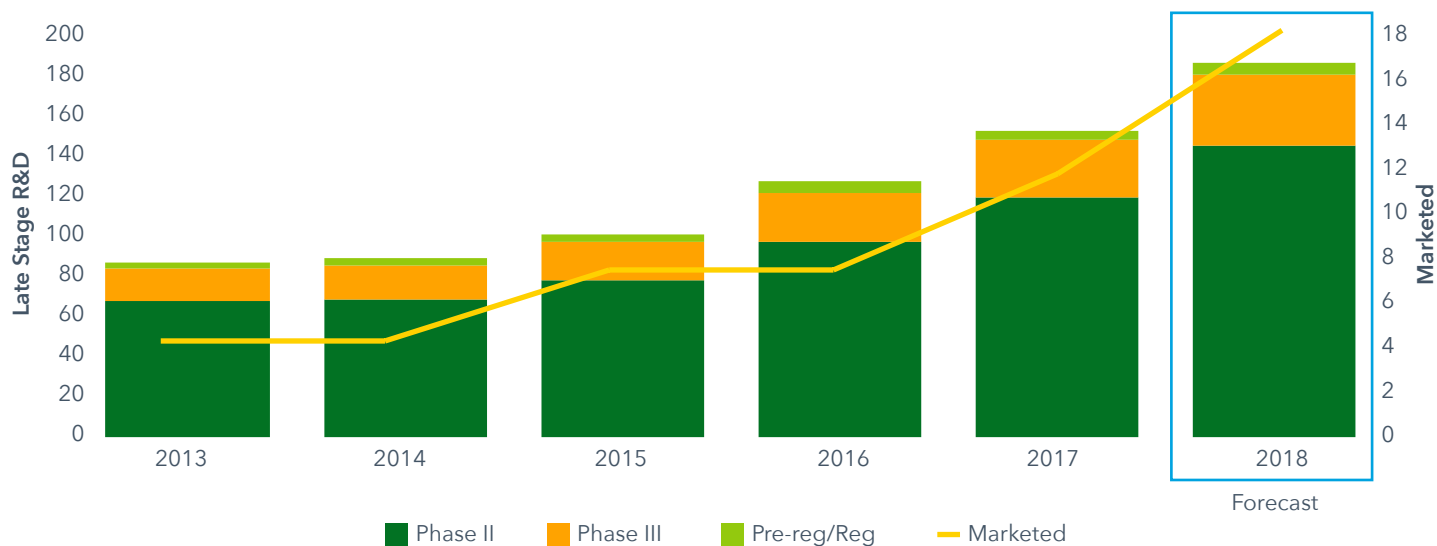
As next-generation treatments become more common, health system budget pressures will increase, and payers will likely limit or reject access to these drugs as they impact budgets. How cell- and gene-based therapies and regenerative medicines are priced and how they are paid for will need to evolve to enable predictability for reimbursement agencies (such as governments and private insurers) and to smooth their financial impact.

**Exhibit 2: Next Generation Biotherapeutic Types and Mechanisms**

GENE THERAPIES			CELL THERAPIES
Adeno-associated virus-based gene therapy	Genetic therapy	Plasmid-based gene therapy	Cell engineering
Adenovirus-based gene therapy	Genetically engineered autologous cell therapy	Retrovirus-based gene therapy	Cell transplantation
DNA vaccines	Genetically engineered autologous cell vaccine	Targeted gene repair	Somatic cell therapy
Gene expression regulation	Herpes virus-based gene therapy	Tumor suppressor genes	Stem cell therapy
Gene technology	Lipid-based gene therapy	Viral vector-based gene therapy	Stem cell transplantation
Gene transfer system	Non-viral vector-based gene therapy		Tissue engineering
			Tissue regeneration
			Tissue therapy
			Xenogeneic transplant

Source: IQVIA Institute, Feb 2018

**Exhibit 3: Number of Next Generation Biotherapeutics Currently Marketed or in Late-Stage Pipeline**



Source: IQVIA Institute, IQVIA R&D Insight, Jan 2018  
 Notes: Reg = Registered.

### IMPLICATIONS

The challenge for both manufacturers and payers will be to create a new payment and reimbursement paradigm that maximizes the access to these clinical advances. Curing a patient with a single treatment does not provide a continuing flow of revenue for a life sciences company, and as a result, one might expect these therapies to be set at a higher price, which then must be paid for at time of delivery. The concentration of those costs in a much shorter period presents challenges for payers that cannot be easily addressed. With some earlier examples of next generation products like sipuleucel-T (Provenge), the cost of the treatment, incurred in a single calendar month, created a ‘cost-density’ which was additionally prohibitive to some patients and providers in the United States. With each new instance of these novel medicines, the balance of cost and value must be revisited but is additionally complicated by the varying ways in which costs are incurred over time. The uncertainty about access, and perhaps return on investment, contributes further pressure for manufacturers to set prices as high as the market will accept.

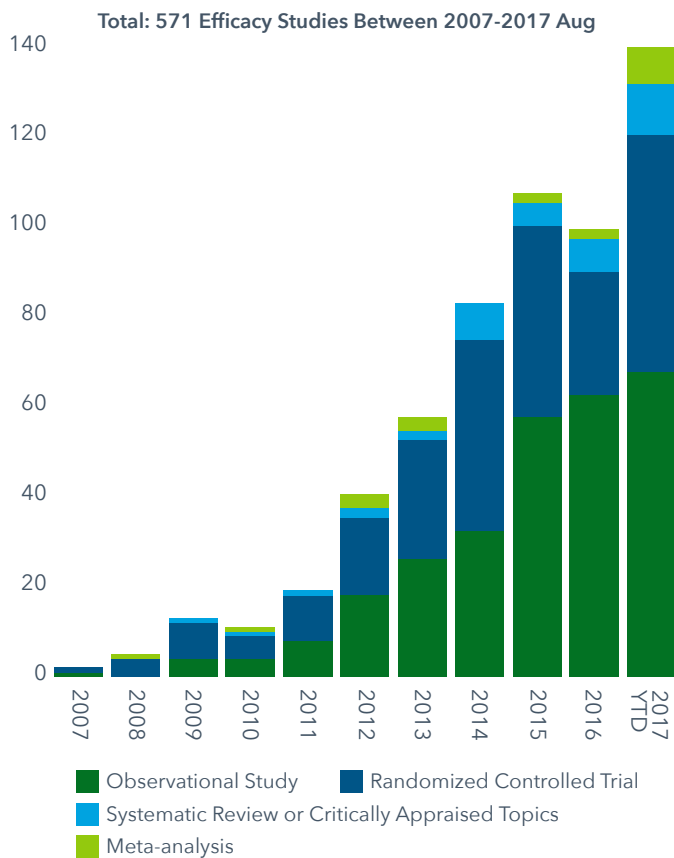
In most cases, these new medicines will have costs approaching or exceeding \$100,000 per patient, and those launched to date have been used in fewer than 500 patients per year. These costs will generate payer concerns if large numbers of patients begin to be treated, and lead them to add access restrictions. While the flow of Next Generation Biotherapeutics is increasing, payment models have been slow to adapt. In the future, governments, insurers and patients will not be able to afford Next Generation Biotherapeutics without some mechanism to adjudicate which patients are eligible for treatments, negotiate payment based on outcomes or to amortize costs over time.

# Apps make their way into treatment guidelines

## BACKGROUND

The proliferation of Digital Health tools, including mobile health apps and wearable sensors, holds great promise for improving human health. As with other new health technologies, evidence of their effectiveness is a fundamental requirement of the health system and a limiting first step to adoption into clinical practice. Although analyses of the Digital Health landscape published by the Institute in 2013 and 2015 found evidence still to be scarce and the value of Digital Health difficult to measure, this has now changed and the benefits to patients are becoming more clear.<sup>10</sup>

**Exhibit 4: Number of Published Digital Health Efficacy Studies over Time**



Source: IQVIA Institute for Human Data Science. The Growing Value of Digital Health: Evidence and Impact on Human Health and the Healthcare System. Nov 2017

The growing acceptance of apps in healthcare is lagging behind popular culture as a direct result of the need to prove value with evidence, and ensure integration into provider workflows. The vast numbers of apps that were initially developed have proven to be ill-suited to task. As app designs have iterated and improved, a collection of leading apps has emerged along with an accelerating trend towards proving health value. An emerging adoption of apps into clinical practice is now underway, as seen by a growing body of published evidence that included 571 digital health studies from 2007 to August 2017 (see Exhibit 4).<sup>10</sup>

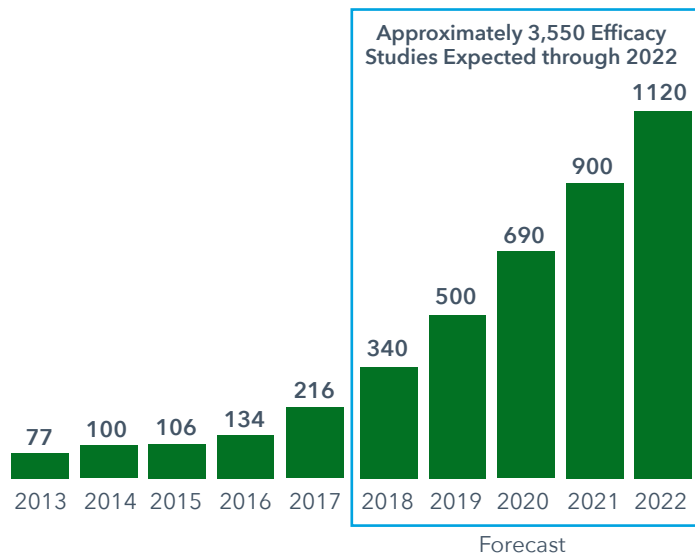
## OUTLOOK FOR 2018 AND BEYOND

In 2018, we expect approximately 340 digital health efficacy studies will be completed and published, continuing the trend of building hard evidence to support digital tools and interventions (see Exhibit 5). These will span a broad range of diseases, with large-population chronic diseases like diabetes and heart disease that benefit from patient self-management, behavioral support or intervention leading the way. We also expect this trend to continue over the next five years, growing by approximately 3,500 studies, as new uses are found for digital health apps and the digital biomarkers they sometimes track.

This growing amount of evidence will increasingly be incorporated into practice guidelines. Responding to the strengthening body of evidence supporting apps, major professional groups will begin to incorporate apps into their practice guidelines, following the lead of the American Diabetes Association (ADA). The ADA just recently included technology-enabled (e.g., app-supported) diabetes self-management solutions in their 2018 clinical guidelines recommendations (National Standards for Diabetes Self-Management Education and Support [DSMES]),<sup>11</sup> while the American College of Cardiology (ACC) has identified digital health, big data and precision health as three focus areas for their recently released 2018 innovation roadmap.<sup>12</sup> Other groups will likely follow quickly with guidance on the use of apps, especially incorporating them into clinical



## Exhibit 5: Projected Growth of Digital Health Published Evidence



Source: IQVIA AppScript Clinical Evidence Database, Feb 18, 2018; IQVIA Institute, Feb 2018  
Notes: 2018 data and growth in efficacy studies extrapolated from growth trend. Historical numbers updated since original publication based on database update.

guidelines and protocols, helping such app-supported programs gain accreditation and reimbursement.

It is not surprising that these therapy areas are the first to find adoption within the clinical community. Diabetes, depression and anxiety have been found to be the leading areas in terms of evidence that supports app usage.<sup>10</sup> For diabetes, evidence of benefit spans both prevention and management, while in the cardiovascular space, there has been evidence of impact for digital-app-supported cardiac rehab. Additional evidence in asthma and pulmonary rehab may encourage medical associations in this space to additionally express their views.

Further initiatives also indicate growing efforts to fit apps into practice and growing acceptance by clinicians and policymakers. The joint collaborative, Xcertia, founded by the American Medical Association, American Heart Association, DHX Group and the Healthcare Information and Management Systems Society (HIMSS), was formed with the goal of generating

standards for app development, particularly around privacy. The American Heart Association, while not yet issuing specific guidelines, has formed the AHA Center of Health Technology and Innovation, which was announced in October 2017. This center will integrate guidelines with digital healthcare solutions from industry.<sup>13</sup>

The development of a common set of best practices for systems design and integration, privacy and a focus on robust evidence-based approaches will help encourage investment in apps generally and raise the quality of apps that are developed. The greater alignment emerging across these diverse stakeholders is paralleling the evolution of functionality, design, and the burgeoning evidence basis for apps.

### IMPLICATIONS

In the constant struggle to better engage with patients, the emergence of well-designed apps and mobile devices offers the potential to break down barriers and improve outcomes for patients sometimes at near-zero incremental costs. Alignment on the appropriate sets of features and safeguards has taken some time to emerge but is now in place, and technology innovators are advancing into the field in significant numbers. The need for regulatory clarity will be a key foundation upon which further investments and wider adoption will be based. The FDA's continued focus on and openness to apps is therefore critical to the future of app developments, and that is in turn conditional on the continued flow of validated clinical efficacy studies. The next level of adoption depends on high-quality apps, robust clinical trial evidence, robust patient privacy, and curation of the plethora of apps to enable providers and patients to make informed choices. There will be significant further advances in app functionality and integration with provider workflows in the next five years which will be critical to stakeholder adoption. These issues are connected as the availability of efficacy evidence aids curation and app selection, and the more that apps are selected based on criteria that are familiar from other healthcare decisions, the easier adoption becomes for regulators, providers, payers and ultimately patients.

**AREAS OF INNOVATION**

# Telehealth usage broadens

**BACKGROUND**

It has long been suggested that rising healthcare costs can be offset by addressing inappropriate use of primary care, urgent-care clinics and emergency rooms (ERs). Around the world, some countries have already made considerable progress using a mix of phone and internet consultations to attempt to siphon off patients who could be described as misusing resources and encourage them to go to a more optimal site of care, or just stay home. Advocates of telehealth argue that most of the reasons to see a provider in person can be supported remotely, including capturing vital signs, and patient reported metrics such as quality of life, pain thresholds, etc.

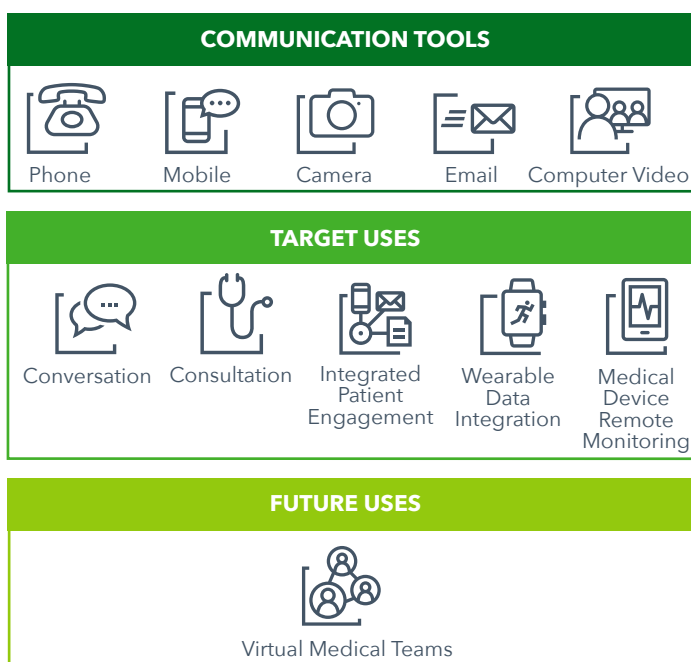
Policies that encourage ‘right behaviors’ or discourage the wrong ones have made some inroads, such as reimbursing providers less if they fail to reduce ER

utilization or readmissions. Setting patient copayments higher for undesirable activities is an approach that payers have used, and some insurers are now disallowing ER reimbursement for certain events that could have been handled more cheaply, elsewhere. The cost differences are significant: an ER visit averages \$1,200, while an urgent care clinic visit averages 10% of that, an office visit or an in-store pharmacy clinic may cost \$50-\$150 and telehealth visits can cost \$50-80.

**OUTLOOK FOR 2018 AND BEYOND**

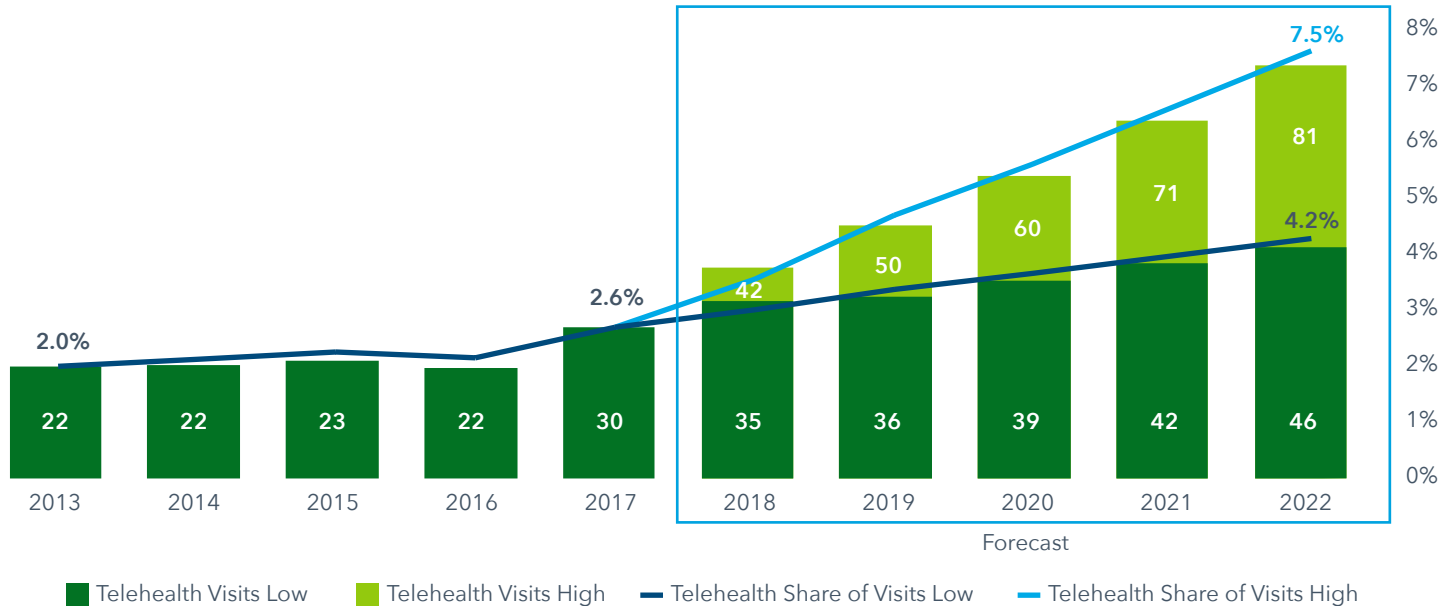
In 2018, telehealth visits may increase by 15-40% and account for 35 to 42 million visits, nearly double the steady level seen from 2013–2016 (see Exhibit 7). By 2022, if the pace of adoption continues to accelerate, as many as 7.5% of visits would be telehealth, while even modest continued growth would see telehealth 50% larger than current levels in five years. In 2018, virtually all large private employers will offer telehealth services to their beneficiaries and begin to offer even larger financial incentives to use them, and many are promoting them with television campaigns.<sup>14,15</sup> For many larger employers, telemedicine is shifting from a convenience perk for employees to a replacement for some primary care and urgent treatments and is being incentivized with low or no copays and a greater focus on the patient experience. Varying sources suggest that telehealth is available to between 40 and 90% of privately insured beneficiaries in the United States, but very few patients currently use these services. Overall, the addressable market of ambulatory visits that could be shifted to a lower-cost venue is approximately 400 million visits per year, which includes ER, urgent care and primary care visits that could be shifted from in-person to telehealth visits.

**Exhibit 6: Telehealth Communication Methods and Uses**



Source: IQVIA Institute, Oct 2017

## Exhibit 7: U.S. Telehealth visits 2013–2022



Source: IQVIA National Disease and Therapeutic Index, Jan 2018; IQVIA Institute, Feb 2018

### IMPLICATIONS

To date, the United States has had only limited adoption of telehealth, with barriers centered on payers' concerns about the legitimacy of a virtual visit, patient concerns about being treated by a random doctor, and providers' concerns about being paid for their time. Health systems which carry financial risk, such as Accountable Care Organizations (ACOs), have a vested interest in the success of these approaches, as do health insurers if they can benefit by keeping sponsors' costs down. Once a patient uses telehealth, seamless integration with real-world providers and the patient's insurance are key to ensuring appropriate care, avoiding duplication in treatment and achieving the fullest savings. With the wider adoption of EHRs, and the penetration of high speed internet and mobile devices, new technology is making it possible to address many of these concerns. At the same time, the consolidated payer and provider landscapes now mean that more organizations have the motive and opportunity to drive greater use of telehealth, and change is occurring rapidly.

An inappropriate in-person patient visit is vastly more expensive than an inappropriate virtual visit, so even some level of induced demand is likely acceptable so long as overall costs are reduced. Rising healthcare costs may be addressable by encouraging the right patients to forego in-person visits to primary care, urgent-care clinics and emergency rooms. By offering a phone call or video-chat, often with substantially lower copayments, the convenience and cost savings are expected to drive large numbers of patients to change their behaviors. Every patient will likely experience some form of telehealth engagement within the next five years.

## SPENDING GROWTH DRIVERS

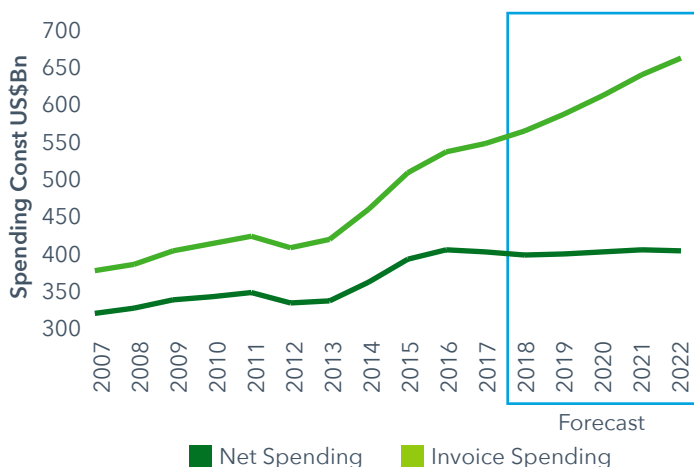
# Branded medicine spending in developed markets falls

### BACKGROUND

Over the past five years, branded drug net spending in developed markets has risen from \$326 billion to \$395 billion. This compares to invoice spending which rose to \$541 billion in 2017 from \$401 billion, five years earlier (see Exhibit 8). The use of off-invoice discounts and rebates along with statutory price concessions required of manufacturers by governments or government programs result in net spending which is \$146 billion lower than invoice, and that difference has nearly doubled in the past five years.

In total, 87% of the \$69 billion of net growth has come from the United States. In other developed markets, (Japan, Germany, France, Italy, Spain, United Kingdom, Canada, South Korea and Australia) where largely single-payer systems manage costs and prices, growth has been slower or declined since 2012. New brands drove the unprecedented growth in spending in 2014 and 2015, from the combined effects of new and highly effective treatments for hepatitis C, a number of cancers and other diseases.

**Exhibit 8: Developed Market Brand Invoice and Net Spending 2007-2022**



Source: IQVIA Market Prognosis Sep 2017; IQVIA Institute, Oct 2017

Notes: Developed markets include: U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia.

### OUTLOOK FOR 2018 AND BEYOND

In 2018, net brand spending will decline in developed markets by 1-3%. This has the effect of reducing net spending overall on brands in developed markets by approximately \$5 billion to a total of \$391 billion in 2018. Over the next five years, net brand spending will remain flat, despite the expected entry of new, branded medicines; the overall impact on payers being the same in 2022 for brands as in 2017.

The next five years from 2018 to 2022 will see:

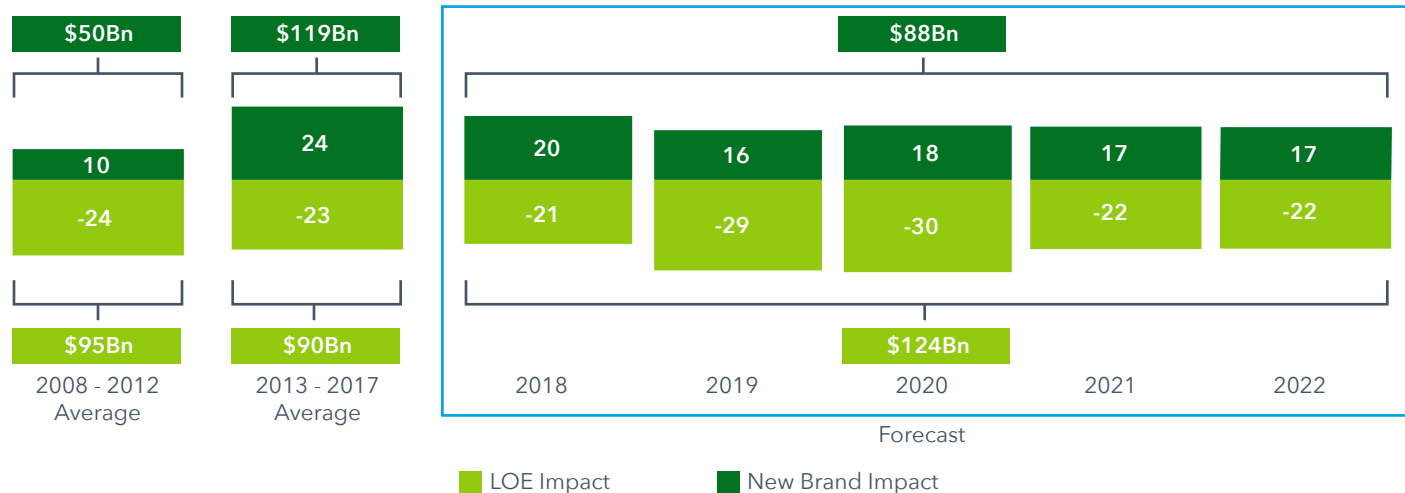
**Patent expiry** impact will be 37% larger than the prior five years, including both small molecule and biologics; the peak year of impact is expected to be 2020 when spending on brands that no longer have exclusivity will be reduced by over \$30 billion across the ten developed markets (see Exhibit 9).

**New medicines** growth will be slower in 2018-2022 than the period from 2013-2017 (see Exhibit 9) but growth from new medicines will still be above the 2008-2012 average. In prior years new drugs accounted for 2-3% of brand spending, with notable exceptions for over nearly 7% in 2015 when new hepatitis C drugs were widely used. From 2018-2022 there will be 40-45 new active substances launched per year and new medicines growth will drive 2.5-3.5% of brand spending in developed markets.

**Net price levels for branded drugs** will rise modestly in the United States at 2-5% per year but will fall in other developed markets.

**Volume for existing branded and generic medicines** will remain slow, with the ongoing shifts towards newer medicines over time.

### Exhibit 9: Developed Markets New Brand and Brand Loss of Exclusivity Impact on Growth 2008-2022



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute Oct 2018

Notes: Developed markets include: U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia; LOE = loss of exclusivity.

#### IMPLICATIONS

While the absolute share of spending from new medicines may be small, control of pricing and access to new drugs is a key point at which payers can influence drug spending trends for the longer term. New drugs will continue to be developed and launched, but the inherent unpredictability that surrounds them is driving ever greater caution amongst payers. The lack of growth on brand spending in markets outside the United States will be achieved by payers’ ongoing and aggressive management of access and uptake of a robust pipeline of new medicines.

Across the developed markets, payers will be spending the same or less on innovative medicines over the next five years. The United States is likely to be the one outlier among developed markets, with brand net spending growth expected at 1–4% through 2022; this contrasts with flat trends in the other developed markets and declines in Japan. The steady level of spending will provide opportunities for payers to focus on addressing outstanding healthcare disparities, to increase access or to invest in approaches to address system inefficiencies.

## Specialty medicines drive all spending growth in developed markets

### BACKGROUND

The past decade has seen a sustained shift in the focus of new medicines towards specialty pharmaceuticals. These are defined as those medicines treating chronic, complex or rare conditions and also meeting a majority of seven additional criteria which reflect varying interests of stakeholders. Specialty medicines may have costs exceeding \$6,000 per year, or require some form of payment assistance. They also may require special handling in the supply chain, or use highly specific distribution arrangements. Some medicines are considered specialty because they require administration by a healthcare provider or are initiated by a specialist, or because there may be significant side-effects or treatment counseling required.

Driven by new therapies and slowing or declining growth of traditional medicines, specialty share of global spending has risen from 19% in 2007 to 32% in 2017. For the tenth consecutive year, specialty medicine growth exceeded traditional medicines in developed markets (see Exhibit 10). In the ten developed markets, specialty represented 39% of spending in 2017, totaling \$297 billion, led by five major European countries (France, Germany, Italy, Spain, United Kingdom) and the United States, all with specialty share above 41%.

### OUTLOOK FOR 2018 AND BEYOND

In 2018, the \$318 billion of specialty medicines will represent 41% of developed market spending, up from \$172 billion in 2013.

Specialty will contribute all of the growth in medicine spending in 2018, offset by declines in traditional medicines (see Exhibit 10). Specialty medicines reflect a wide range of therapies ranging from cancer, autoimmune diseases and antivirals for hepatitis C. Ten drug categories account for 81% of specialty spending, while another 46 categories make up the remainder (see Exhibit 11). Oncology and autoimmune biologics lead the specialty categories, accounting for 46% of 2017 spending and 68% of projected growth in the next five years. Antiviral treatments, including those for hepatitis C, were significant drivers of growth in the last five years but are projected to decline, as many patients have already been treated (and cured).

Specialty share in developed markets will continue to rise, albeit more slowly than the last few years, and surpass half of medicine spending in 2022 in the United States and in four out of the five key European countries: France, Germany, United Kingdom and Spain.

**Exhibit 10: Brand Spending Growth of Specialty and Traditional Drugs 2013-2022 in the Developed Markets**

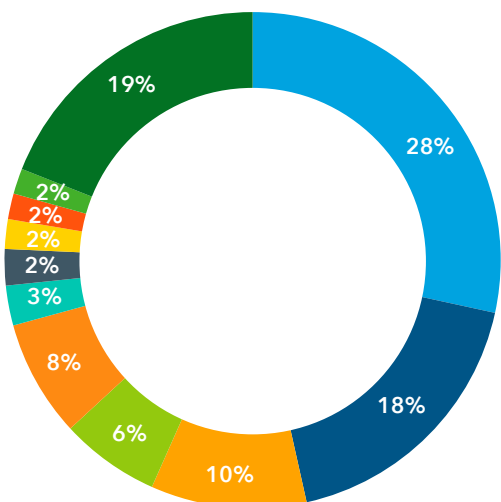


Source: IQVIA Institute, Oct 2017

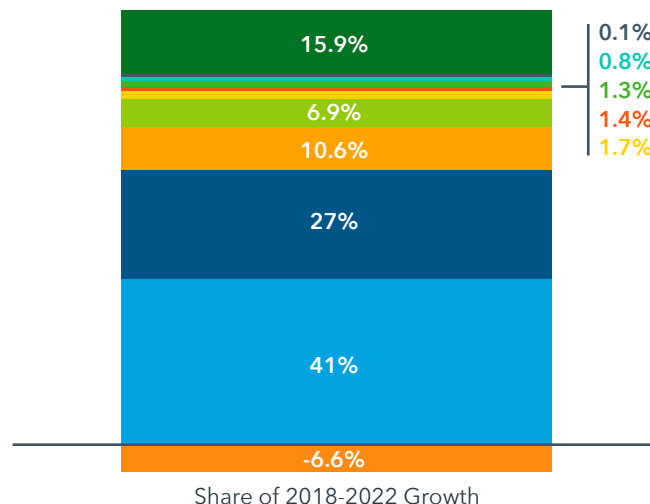
Notes: Developed markets include: U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia.

## Exhibit 11: Specialty Medicines Spending and Growth in Developed Markets

Share of 2017 Developed Markets Specialty Spending \$297Bn



Developed Markets Specialty Spending Growth 2018-2022, \$140-150Bn



■ Oncology ■ Autoimmune ■ HIV ■ Immunosuppressants ■ Antivirals ■ GM-CSF  
■ ESA ■ AMD ■ Blood Coagulation ■ Poly IVIG IV/IM ■ Others

Source: IQVIA Institute, Oct 2017

Notes: GM-CSF = Granulocyte-macrophage colony-stimulating factor; ESA = Erythropoiesis-stimulating agents; AMD = Age-related macular degeneration.

### IMPLICATIONS

The growth of spending on specialty medicines will be constrained by cost and access controls and a greater focus on assessments of value; however, specialty is still expected to reach 48% of spending in developed markets by 2022.

Payers' ability to negotiate lower net costs is often related to the presence of direct competition, either other branded originators or generic or biosimilars, whereas specialty drugs generally have fewer direct competitors. While significant levels of off-invoice discounts and rebates are common, especially for traditional medicines, they are understood to be lower for specialty medicines, partly due to these dynamics. Faced with the prospect of limiting access or paying rising costs, there are few simple choices for payers.

Providers are already experiencing rising administrative requirements from payers to justify each patient's use of these medicines and these will continue to increase. In some geographies, providers have devolved budget responsibility, as in parts of Europe and with accountable care organizations in the United States; providers must balance the needs of each patient with the budget impact across the whole covered population.

Manufacturers have been shifting their research to focus on specialty, and while populations are smaller, clinical benefits are greater and the individual patient costs higher; the growing resistance of payers to rising spending means that some of these medicines may not produce significant financial returns.

## SPENDING GROWTH DRIVERS

### Slower growth in China and other pharmerging markets

#### BACKGROUND

The share of global medicine spending from pharmerging markets has risen from 13% in 2007 to 24% in 2017. This corresponds to an increase in spending from \$81 billion in 2007 to \$270 billion in 2017, with an average rate of 12.8%, more than twice the rate of global growth.

Pharmerging countries are defined by the IQVIA Institute based on per capita income below \$30,000 and a five-year aggregate pharmaceutical growth over \$1 billion. This definition reflects the intersection of health systems that are growing because of unmet medical need and where growth has acted as an incentive for life sciences companies to invest in addressing those needs. The growth in spending seen in the pharmerging markets from 2007–2017 was driven both by governments’ efforts to expand access to healthcare for their people and by the investments of

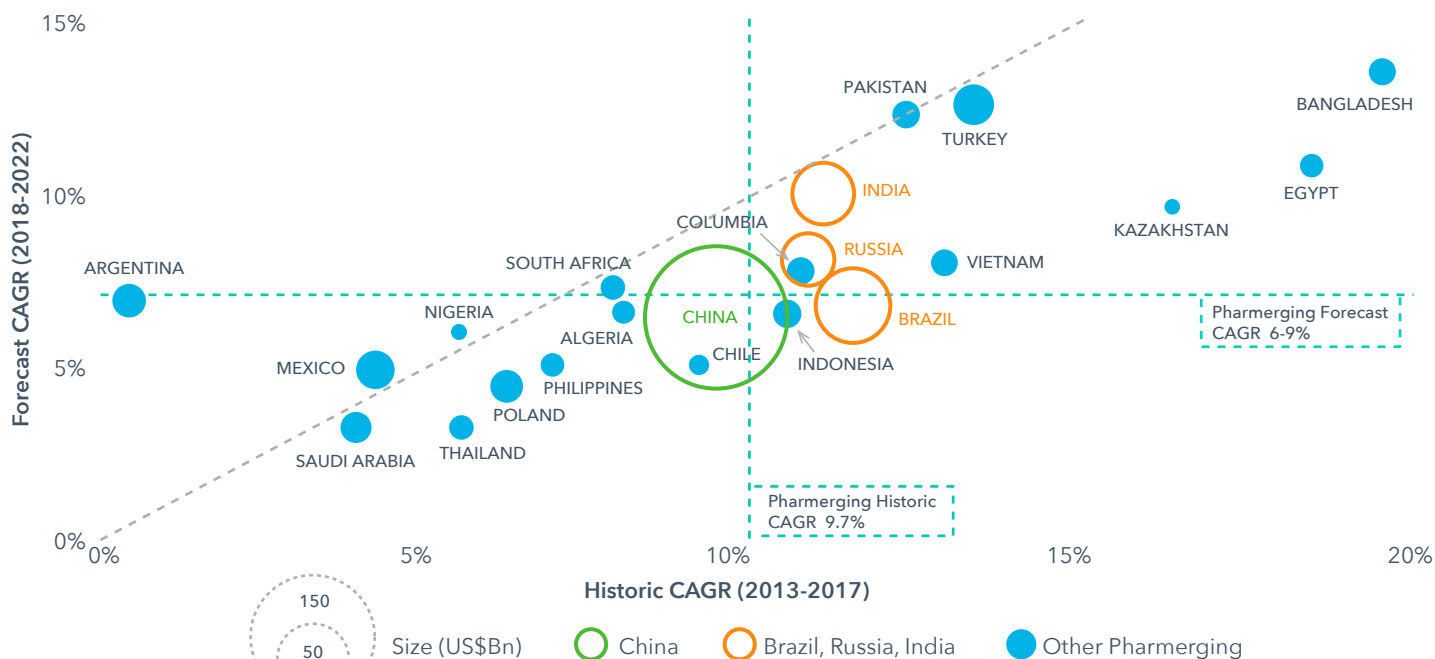
multinational manufacturers who expanded operations, acquired or partnered with local companies and significantly expanded their revenues from these countries.

The majority of medicine use and spending in these countries continues to be for generic medicines, and payment continues to be predominately out of pocket for consumers, ultimately tying medicine spending growth to economic growth of their overall economies (see Exhibit 12).

#### OUTLOOK FOR 2018 AND BEYOND

Pharmerging markets will be driven by volume changes and the use of generics and will grow by 7–8% in 2018, down from the 9.7% compound annual growth rate over the prior five years and marking the third year that growth will be less than 10%. The pharmerging markets are projected to grow by 6–9% to \$345–375 billion by 2022. China is the largest pharmerging country but will grow by only 5–8% over the next five years to reach \$145–175 billion in 2022.

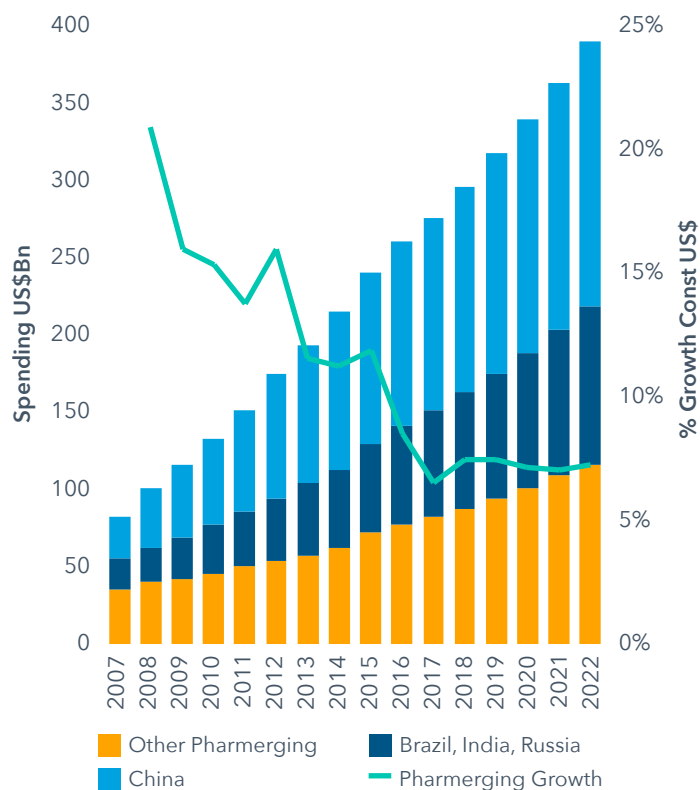
Exhibit 12: Pharmerging Spending Growth by Country



Source: IQVIA Market Prognosis, Oct 2017



### Exhibit 13: Pharmerging Spending and Growth



Source: IQVIA Market Prognosis, Sep 2017

Faster growth is expected in India at 9-12%, Russia at 7-10% and the remaining smaller pharmerging markets will average 6-9%. Spending in India will continue to grow enough to have it rise into the top ten countries in 2018, and to the ninth largest in 2019 through 2022.

Over the past four years, Argentina had been experiencing economic disruption and very high local currency price growth. When reported in US\$, the growth is substantially lower. In the next five years, growth will be driven by the continued implementation of universal healthcare and an aging population and offset by a relatively modest economic recovery. Mexico and Nigeria, where the rate of growth differs by 1% or less, should not be characterized as having an acceleration.

Decelerating spending growth in China, Brazil, India and Russia mirrors slowing economic growth in these countries; this impacts medicines given high patient out-of-pocket costs. Of particular importance in China is the new Generics Quality and Efficacy Evaluation guidelines which are intended to drive the registration and development of bioequivalent generics. Currently, off-patent originators account for about 18% of spending in China and estimates range from 50-85% of that spending could shift to bioequivalent, locally-produced generics within the next five years.

#### IMPLICATIONS

Slowing rates of growth will allow governments to better manage budget exposure, which will be welcome, but will also limit inward foreign investment. The slowing rates of growth are also the result of policies directly designed to achieve that result. In China and other pharmerging markets, policies to negotiate prices for higher cost drugs, to encourage generic use and domestic manufacturing are all part of the range of approaches countries are using to generate predictability in their exposure to healthcare costs. Achieving full access to healthcare for most pharmerging markets is a complex balance of encouraging investment while also discouraging growth that makes medicine unaffordable to individuals. Furthermore, if U.S. tax reforms enable profit repatriation, more limited growth opportunities in the future for multinationals in pharmerging countries could see some companies disinvest to bring profits to invest in the potentially more attractive U.S. market. Health system advances in pharmerging markets, to the extent that they rely upon commercial enterprise will depend more on domestic and regional companies than multinationals, and this in turn may be exactly the intent of some countries' policies. Overall, the progress of advancing global health will continue; however, the gains in access to medicine over the past decade will not continue at the same pace due to limited growth of slowing economic conditions.

## U.S. real net per capita spending on medicines steadies

### BACKGROUND

Public scrutiny of drug pricing in the United States has reached almost daily frequency. In a new era of value-based medicine, the price of a new drug is increasingly weighed against the value it brings and the time has passed when increasing the price of an existing drug is “allowed”.

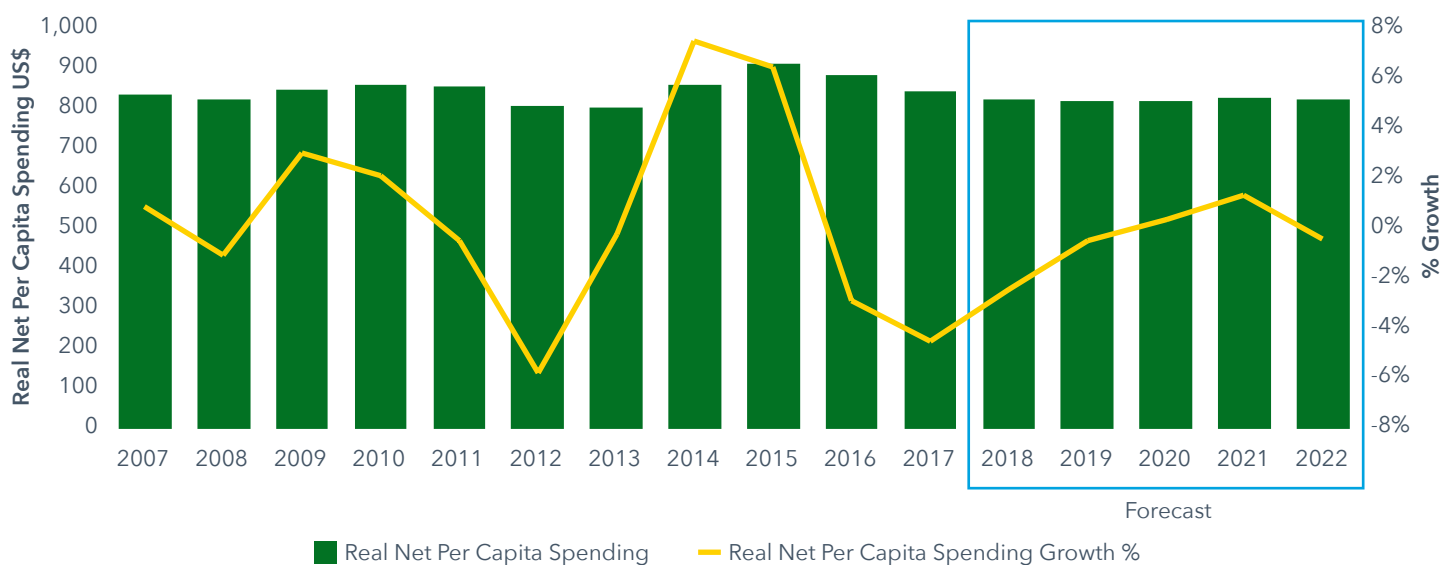
While the vast majority of medicines in the United States are dispensed as generics with patient and health system costs below \$10 for a prescription, a small portion of medicines have costs that are far higher. An increasing proportion of patients have deductible insurance plans or high coinsurance rates that expose them to greater costs. As insurance plans increasingly use patient cost exposure as a feature of benefit designs, high-cost products are discouraged and their lower usage helps balance their overall costs across the covered population.

### OUTLOOK FOR 2018 AND BEYOND

Real net per capita spending on medicines in the United States will decline in 2018 and continue almost unchanged at almost \$800 per person through 2022 (see Exhibit 14). This reflects adjustments for population growth, rising gross domestic product (GDP), and estimates of net manufacturer revenues after off-invoice discounts, rebates and other manufacturer concessions.

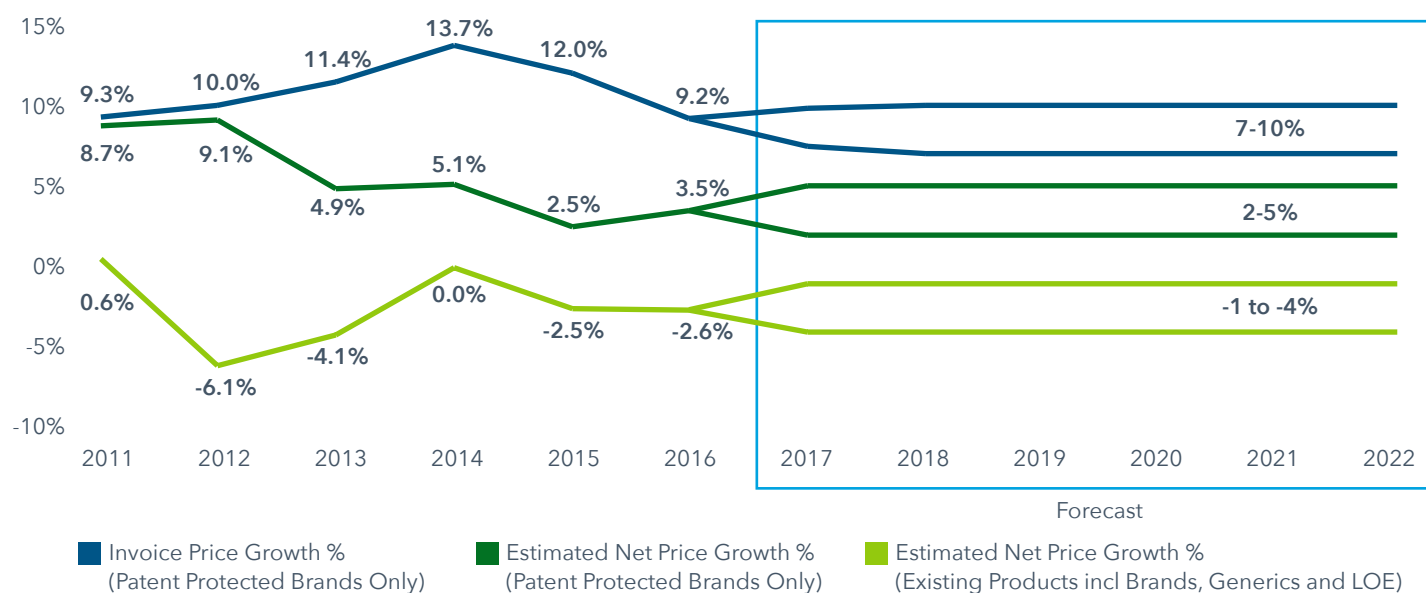
Spending will be unchanged after factoring in the robust pipeline of new drugs, moderating brand price increases of 2–5% on a net basis (7–10% on a list price basis) and the impact of brand losses of exclusivity which is greater in the next five years than the last five. The combination of rising off-invoice discounts and rebates, slowing overall medicine spending growth and a strong economy result in the aggregate adjustment of normalized medicine spending to decline in three successive years following the peak in 2015, and continue almost unchanged to 2022 (see Exhibit 14).

**Exhibit 14: U.S. Real Net Per Capita Drug Spending and Growth**



Source: IQVIA Market Prognosis Sep 2017; US Census Bureau; US Bureau of Economic Analysis (BEA), Dec 2017; IQVIA Institute; Feb 2018  
 Notes: Real medicine spending reflected in 2009 US\$.

**Exhibit 15: US Price Growth Comparing Protected Brands Invoice Price, Net Price and Existing Products Net Price Growth 2011-2022**



Source: IQVIA National Sales Perspectives, IQVIA Institute, Sep 2017

The impact of losses of brand exclusivity continue to offset most growth in spending for branded medicines, while newer, particularly specialty medicines, drive all growth other than price increases. Branded products' losses of exclusivity resulted in \$74 billion in lower brand spending in the past five years but are projected to account for \$105 billion from 2018-2022, peaking at a \$35 billion impact in 2018 (see appendix).

### IMPLICATIONS

While setting price freely has been a unique feature of the U.S. market compared to other countries, the leverage of payers to negotiate net price discounts is effectively offsetting price increases.

High-cost medicines will continue to be launched with headline-grabbing prices above \$100,000 per year, but rarely, if ever, will be used to treat large numbers of patients. Furthermore, multiple attentive stakeholders will significantly limit market uptake of drugs launching with high costs without significant clinical justification or some sort of risk-sharing or outcomes-linked contract.

Drugs which bring only incremental benefits will face an environment that limits patient access—instead favoring existing medicines and generics—and shifts costs to patients to ultimately discourage their use.

As a reaction to these dynamics and the absence of federal legislative action, price transparency initiatives will continue to be legislated only locally with a number of states (e.g., California) mandating transparency. The potential for these laws and the public pressure over the past several years has arguably caused the slowdown in list price increases seen to date.

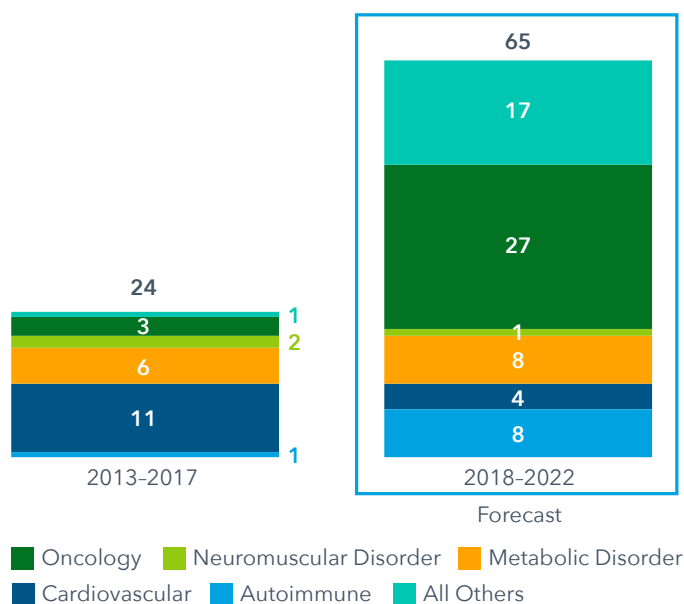
The examples of a few medicines substantially increasing list prices will continue, but are commonly for very low volume drugs or after the ownership of the drug changes hands. While these events have the potential to significantly tarnish industry reputation, they will continue so long as they remain in the interests of each company involved. It is expected that more of these high-cost, low-volume or re-branded therapies will occur each year, even though the aggregate amount of price increases is moderating.

## Outcomes-based contracts find limited role

### BACKGROUND

A medicine’s profile in terms of response rate and benefit on balance means that while some patients do not respond to the treatment, the ones that do justify the cost of the therapy. Historically, this has been a reasonable tradeoff for payers, partly because a non-responding patient could simply stop treatment without incurring substantial costs. Long-term benefits of some newer medicines, such as a ‘cure’ with one shot, or one course of treatment, are often their key features, but those outcomes may not apply for all patients. Recently manufacturer and payer negotiations are including elements of pay for performance for high per-patient cost drugs, at least partly because significant costs can be accrued before a patient’s response can be determined.

**Exhibit 16: Number of New U.S. Publicly Announced Outcomes-Based Contracts and Expected Increase to 2022**



Source: IQVIA Consulting Group, Dec 2017  
 Notes: Publicly disclosed outcomes-based contracts between manufacturers and payers.

The basic framework for an outcomes-based contract codifies a payment model linked to an administrative mechanism to adjudicate the outcome and therefore the value. The most common approach is to attach a discount to outcomes which are worse than those demonstrated in the pivotal clinical trials that are associated with regulatory approval. The contracts result in the balance of the successful outcomes at full price, and the unsuccessful (heavily discounted or free), and generate savings for payers (or providers), as well as provide a degree of predictability for the costs they might incur.

In the United States, these contracts require some level of latitude from the Centers for Medicare and Medicaid Services (CMS) because the discounts would otherwise impact the statutory pricing models in government programs. In the absence of a CMS exception, a money-back guarantee would set the ‘best price’ used in Medicaid pricing at zero, or dramatically lower the average price used in the Medicare Part B pricing formula. CMS has so far demonstrated a willingness to grant these exceptions.

### OUTLOOK FOR 2018 AND BEYOND

It is understood that many outcomes-based contracts have already been negotiated, though many of those are not publicly disclosed for reasons important to both parties. For the ones that are disclosed, the trend is expected to inflect sharply and this is likely also indicative of the patterns for undisclosed agreements. There have been 24 publicly disclosed outcomes-based contracts in the U.S. in the past four years, and this is expected to more than double in next five years. Contracts are being negotiated with both payers and providers, and providers generally skew to those institutions which take on financial risk for achieving outcomes at a certain cost.

In 2018, a range of medicines will seek to link outcomes to payment for a variety of rationales. For example, autoimmune biologics represent one of the most competitive therapy areas comprising a range of diseases from rheumatoid arthritis, Crohn's disease, ulcerative colitis and psoriasis. Due to the competition between brands and the potential for biosimilars to relegate brands to later lines of treatment, manufacturers are seeking to prove their value and link it to payment, as opposed to the more traditional provision of discounts and rebates. Over the past four years, several cardiovascular and diabetes medicines have sought to link payment (and access) to outcomes, at least partly because these therapy areas were well-served by older medicines and payers have substantially limited access to those newer drugs without proven benefits. The largest area of expected increase in these novel contracts are in cancer (and increasingly between providers and manufacturers in that area) and in rare or orphan diseases, where costs for the few patients receiving treatment can reach over hundreds of thousands of dollars.

These contracts come with challenges for both the manufacturer and the party they negotiate with, whether that is a payer or a provider. Key to any successful contract will be the use of easily captured data, adjudicated and verifiable independently, often informed by biomarkers or test results. Some contracts have an ongoing measurement of per patient outcomes, however the administrative burden is high. Other contracts set an annual, or longer, timeframe for the assessment of the value, where the discounts are applicable for the entire timeframe.

By 2022, there are expected to be another 65 contracts agreed to. Most of these outcomes contracts in later years are expected to be in high-cost, specialty medicines, such as cancer or orphan drugs, but some will be negotiated for primary care treatments, which are lower in cost but still large in overall budget impact.

## IMPLICATIONS

Ensuring access for breakthrough drugs will require balancing the concerns and priorities of all stakeholders. Patients could be overburdened with costs, particularly if there are no means-testing mechanisms in place. Providers could face significant financial pressures if they pay up-front for a medicine before uncertain reimbursement and payers ability to control premiums and the overall rise of healthcare costs stretches their predictive powers when faced with high individual cost per patient. Manufacturers should be able to achieve a reasonable return on their risky investments. Mechanisms to adjudicate value and ensure access will be important for all stakeholders, and linking outcomes to payment is increasingly the option of choice.

As the health system evolves a greater comfort with EMRs, as well as wider use of RWD, collecting data for these outcomes requirements will become easier. However, the administrative burden on all parties will escalate and become prohibitive unless the outcomes are designed in measurable ways.

## New wave of biosimilar market opportunity emerges

### BACKGROUND

Biotech medicines, produced through recombinant DNA technology from living cells, can never be exactly duplicated. As such, creating a generic version of biologics is impossible. Regulators, recognizing this, created the similarity threshold and have largely settled on harmonized definitions across developed markets. The part of the market subject to biosimilar competition remains a relatively small part of overall biotech spending because only seven molecules of the 196 currently marketed have faced biosimilar competition, to date. With the total market for biotech medicines reaching \$168 billion across developed markets in 2016, heightened interest is being placed on the role of biosimilars, which is set to expand significantly. There remain a number of challenges with biosimilars, in addition to the intellectual property, litigation, clinical development and regulatory hurdles that seem to be being met by biosimilar manufacturers/companies with a high degree of success and without major issues. Spending on biosimilars is growing, however, the amount of biosimilar spending is still

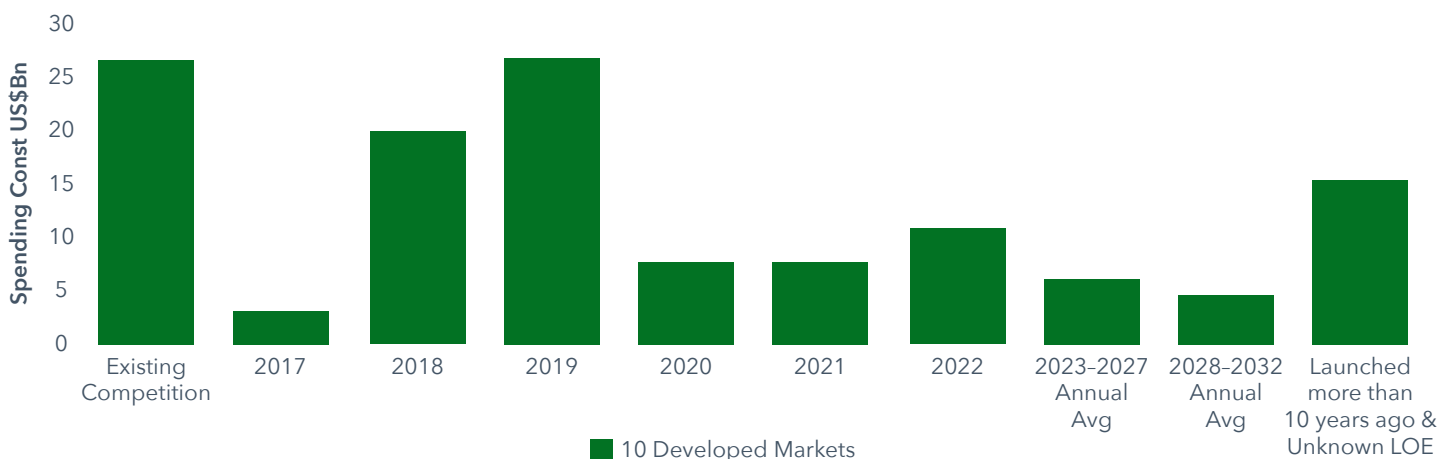
only a small part of the potential opportunity, and the size of the opportunity provides important context for understanding the changes emerging over the next decade for all stakeholders.

### OUTLOOK FOR 2018 AND BEYOND

In 2018, \$19 billion of current biotech spending will become exposed to biosimilar competition for the first time in one or more of the developed markets, significantly greater than the \$3 billion that became exposed in 2017 and adding to the \$26 billion already facing competition. The new exposure to competition in 2018 is the largest single-year change to date and signals the start of the next large wave of biosimilars. From 2019 to 2022, another \$52 billion is expected to face these dynamics for the first time in developed countries (see Exhibit 17), with the United States representing \$37 billion. By 2027, 77% of current biotech spending will be subject to some form of competition.

The timing of competition could be impacted by the uncertainties of developing biosimilars, as well as the potential for litigation. The impact on competitive molecule spending ranges from a 10% increase to a 30% decrease, meaning the \$71 billion exposed to competition from 2018–2022 could result in \$50–78 billion

**Exhibit 17: Biotech Medicine Spending (Newly Exposed) to Biosimilar Competition Over Time, 2016 Values US\$Bn**

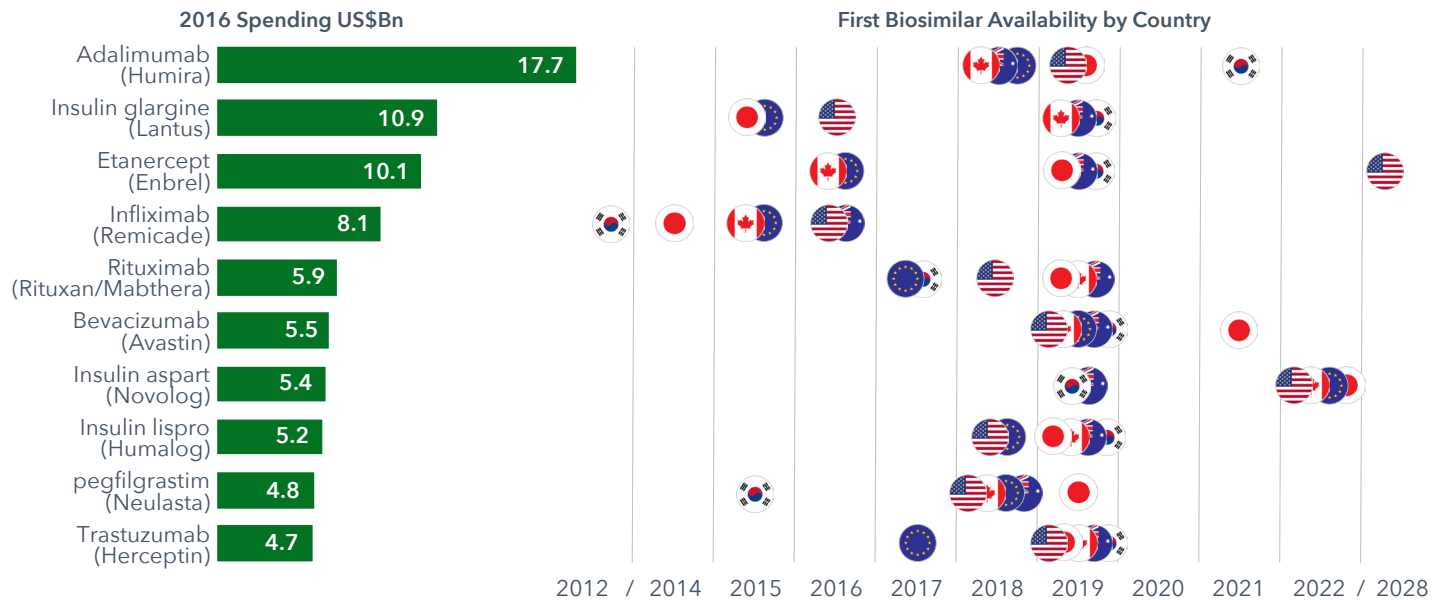


Source: IQVIA Institute, Jan 2018

Notes: Developed markets include: U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia.

LOE = loss of exclusivity.

## Exhibit 18: Developed Markets Top Ten Biotech Medicines Spending and Expected First Biosimilar Availability



Source: IQVIA Institute, Jan 2018

Notes: Developed markets include: U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia.

in spending following biosimilar entry in a variety of likely scenarios. The potential for higher spending could come from incremental demand due to lower prices, or from ineffective competition. The number of competitors and the speed with which they enter the market, and the extent to which they compete on price, will ultimately determine if spending ends up at the lower end of the range.

Patent holders and patent challengers obviously have different expectations, and the courts will no doubt be involved. In some high-profile examples, manufacturers expect courts to uphold their patents for several more years. For example, adalimumab (Humira) could see biosimilars in the United States as early as 2019; however, should one or more of the patents on adalimumab be upheld, out-of-court settlements could see the drug have market exclusivity until 2023. In addition, different rulings across geographies could also mean delays in the United States, even while European biosimilars have historically been available earlier (see Exhibit 18).

### IMPLICATIONS

The benefits of a functioning biosimilar market include expanding access and giving savings back to taxpayers

and other parts of the healthcare or drug budget. One challenge in creating a system of sustainable competition for biologics which could fail if the system of incentives does not ensure that rewards flow to biosimilar makers.

While overall it appears that the next decade will provide sufficient incentives to encourage biosimilar challengers, the greatest uncertainty around biosimilars is whether all of the medicines that can be challenged in the next decade will indeed face competition and from how many companies.<sup>16</sup> Furthermore, dozens of products representing 9% of biotech market spending have already been marketed for more than a decade and have no prospect of biosimilar competition in the next ten years. This is particularly interesting considering the number of large companies, such as Pfizer, Novartis, Amgen, Merck and many other smaller companies active in biosimilars. These long-marketed medicines could be too small to attract interest due to potential manufacturing complexities. Clearly the greater the number of competitors, the greater the competition-induced savings for payers, but only time will tell how much savings biosimilars will generate.

# Notes on sources

## THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

**Market Prognosis** is a comprehensive, strategic market forecasting publication that provides insight to decision makers about the economic and political issues that can affect spending on healthcare globally. It uses econometric modeling from the Economist Intelligence Unit to deliver in-depth analysis at a global, regional and country level about therapy class dynamics, distribution channel changes and brand vs. generic product spending.

**U.S. National Sales Perspectives (NSP)<sup>TM</sup>** measures revenue within the U.S. pharmaceutical market by pharmacies, clinics, hospitals and other healthcare providers. NSP reports 100% coverage of the retail and non-retail channels for national pharmaceutical sales at actual transaction prices. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

**ARK R&D Intelligence<sup>TM</sup>** is a drug pipeline database containing up-to-date R&D information on over 39,000 drugs in development worldwide. The database

captures the full process of R&D, covering activity from discovery stage through preclinical and clinical development, to approval and launch. The information in Ark R&D Intelligence is manually curated by a team of scientifically trained analysts to ensure quality and relevance.

**ARK Patent Intelligence<sup>TM</sup>** is a database of biopharmaceutical patents or equivalents in over 130 countries and including over 3,000 molecules. Research covers approved patent extensions in 51 countries, and covers all types of patents including product, process, method of use and others.

**MIDAS<sup>TM</sup>** is a unique platform for assessing worldwide healthcare markets. It integrates IQVIA's national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and provides estimated product volumes, trends and market share through retail and non-retail channels.

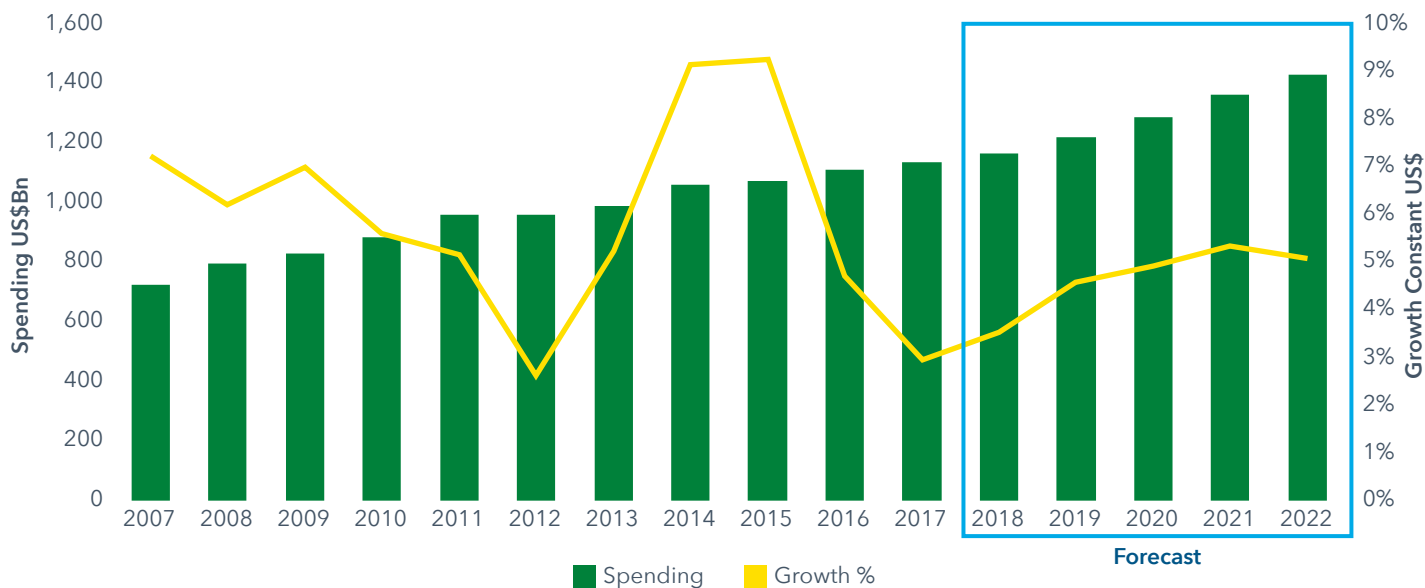


# Methodology

This analysis of medicine spending is based on prices reported in IQVIA audits of pharmaceutical spending, which are in general reported at the invoice prices wholesalers charge to their customers including pharmacies and hospitals. In some countries, these prices are exclusive of discounts and rebates paid to governments, private insurers or the specific purchasers. In other countries, off-invoice discounts are illegal and do not occur. The mix of true prices and opaque pre-discounted prices means the analyses in this report do not reflect the net revenues of pharmaceutical manufacturers. As a part of this report, the IQVIA Institute has compared audited spending data to reported sales, net of discounts, reported by publicly traded companies and made estimates of future off-invoice discounts and rebates. That analysis is referred to as net spending.

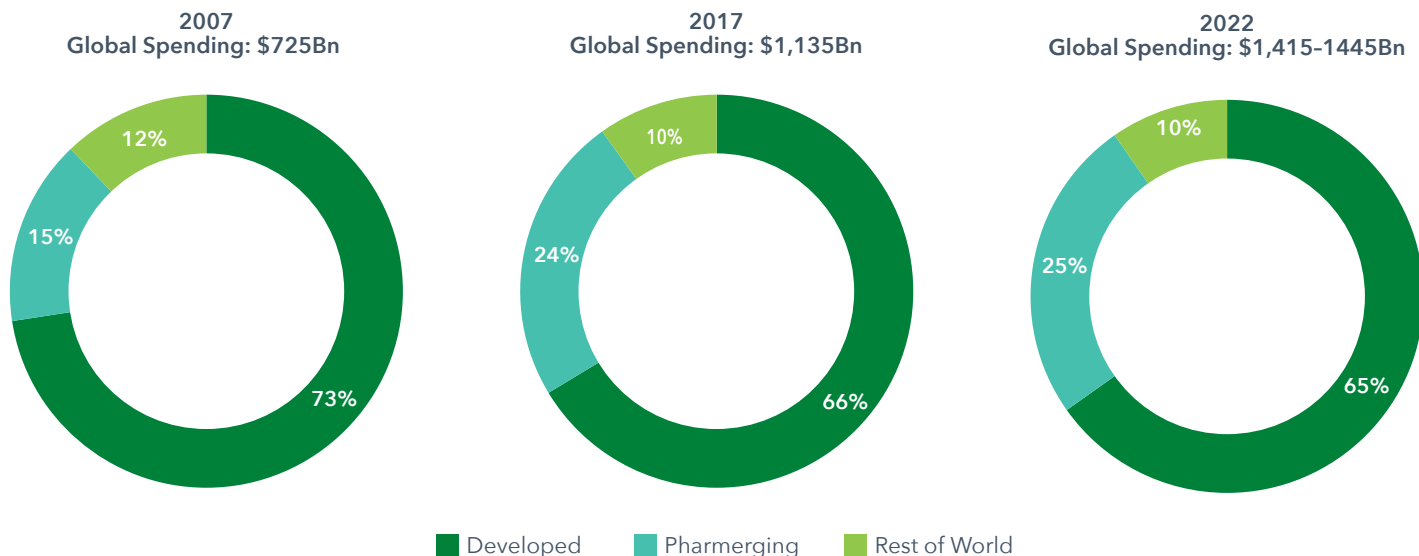
# Appendix

**Exhibit 19: Global Medicine Spending and Growth 2007-2022**



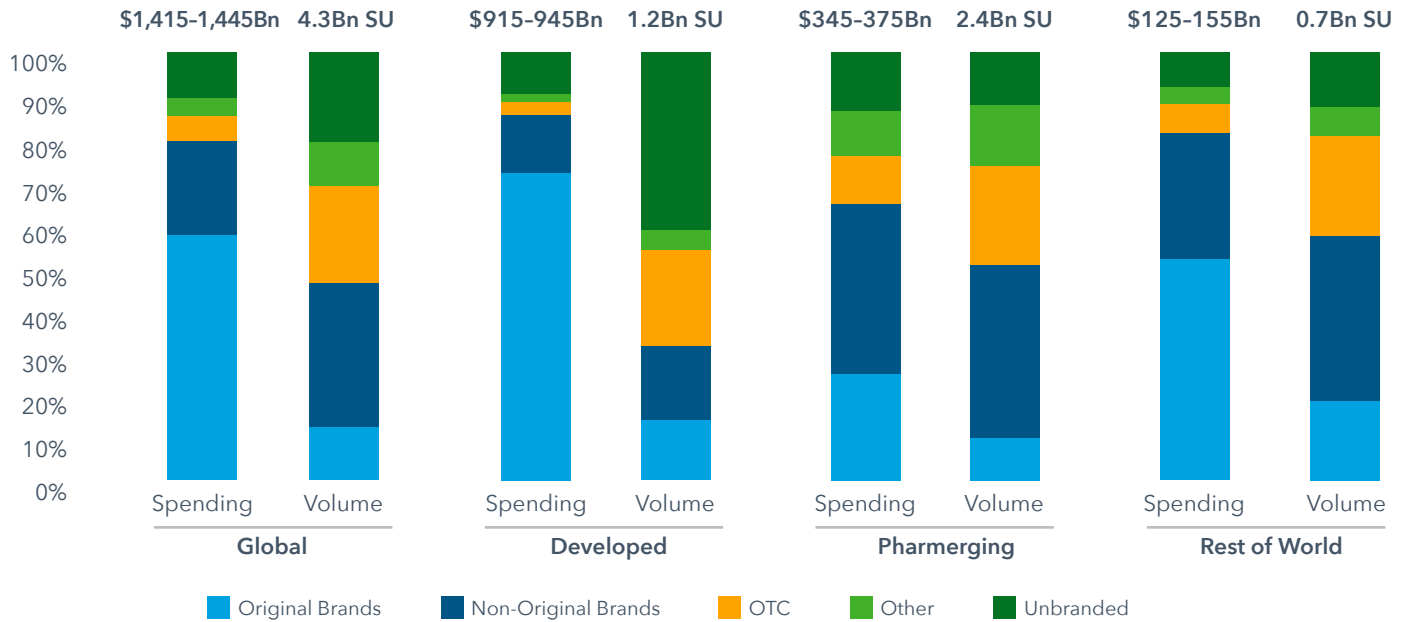
Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017

**Exhibit 20: Global Medicine Spending by Region 2007, 2017 and 2022**



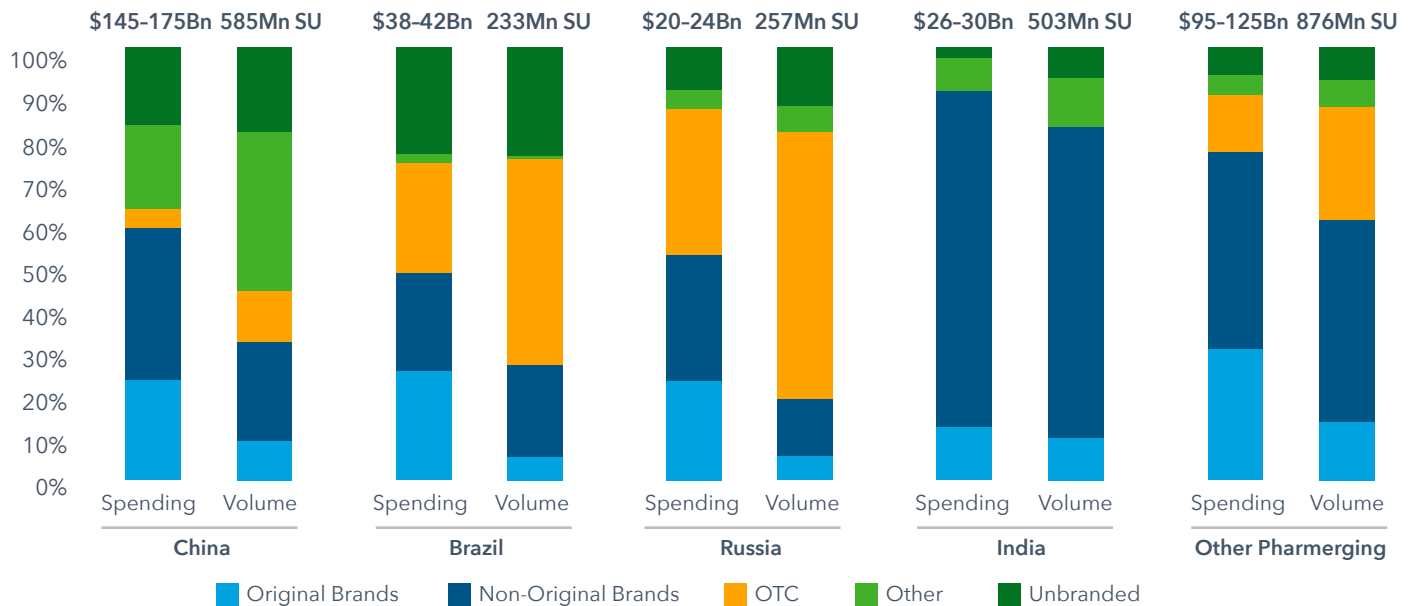
Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017

### Exhibit 21: Global Medicine Spending and Volume by Region and Type, 2022



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017  
 Notes: SU = Standard Units; OTC = Over-the-Counter; Spending in US\$Bn.

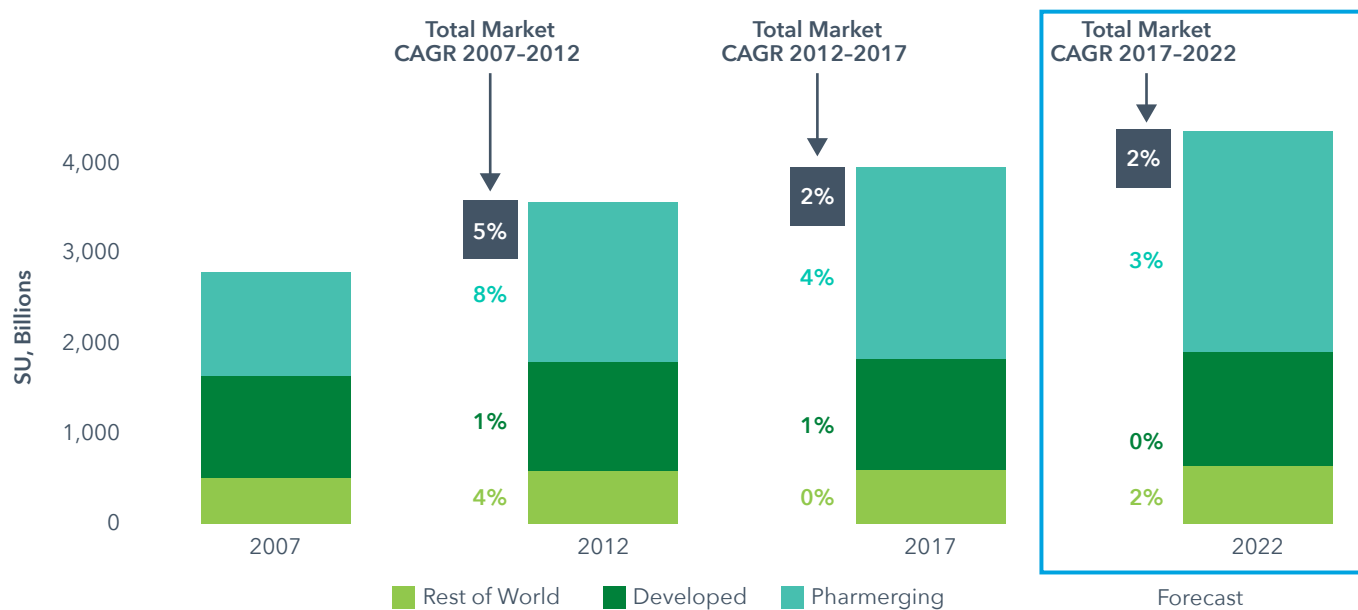
### Exhibit 22: Pharmeringing Medicine Spending and Volume by Type, 2022:



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017  
 Notes: SU = Standard Units; OTC = Over-the-Countries; Spending in US\$Bn.

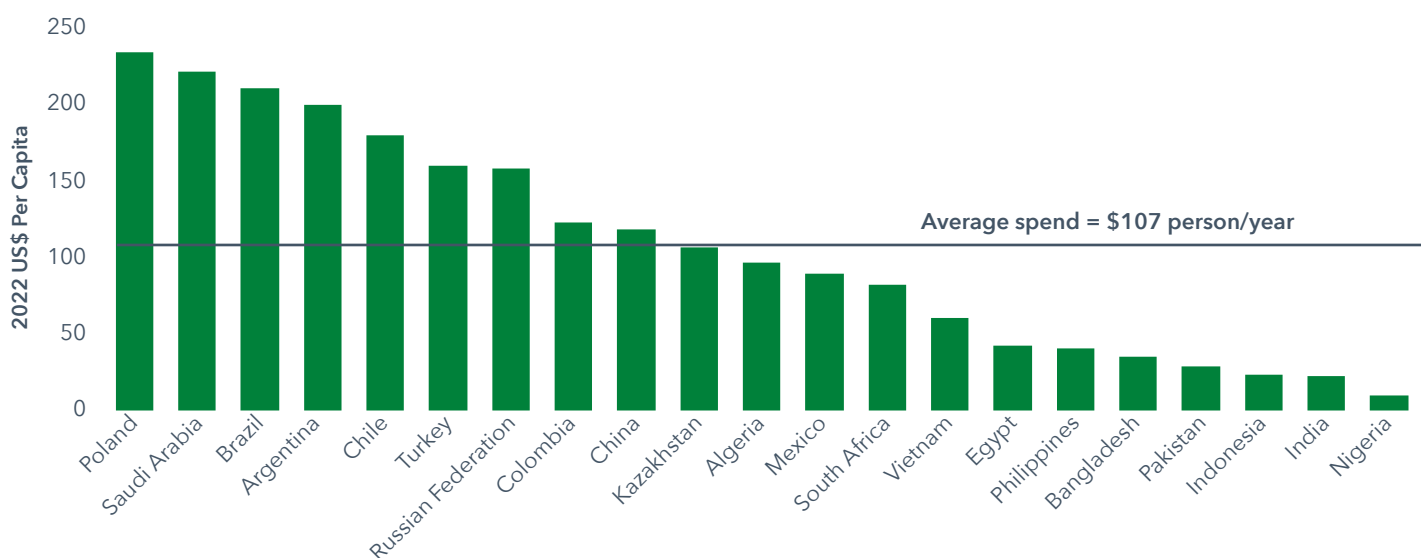
# Appendix

**Exhibit 23: Global Volume in Standard Units, 2007-2022**



Source: IQVIA Institute, Oct 2017  
Notes: CAGR = Compound Annual Growth Rate.

**Exhibit 24: Pharmerging Per Capita Spending by Country, 2022**



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017  
Notes: Spending per capita, per capita growth and overall spending growth in Constant US\$.

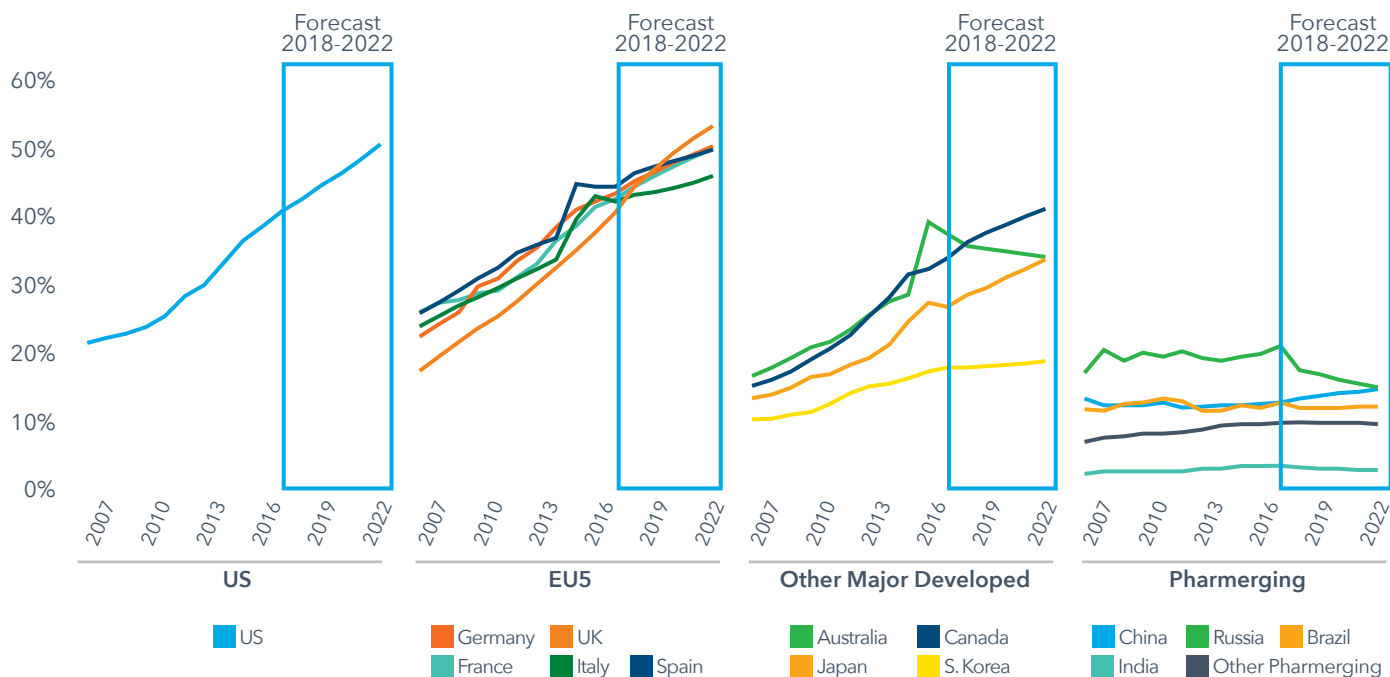
**Exhibit 25: Pharmerging Markets Standard Units Per Capita 2017 and 2022**



Source: IQVIA Market Prognosis, Sep 2017

Notes: SU = Standard Units.

**Exhibit 26: Specialty Medicines Share of Spending by Country, 2007-2022**



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017

# Appendix

**Exhibit 27: Leading Therapy Areas Spending and Growth in Select Developed and Pharmerging Markets**

THERAPY AREAS	2017 CONST US\$ SPENDING	2012-17 CAGR CONST US\$	2022 CONST US\$ SPENDING	2017-2022 CONST US\$ CAGR
Oncology	81.1	11.8%	115-130	7-10%
Diabetes	72.2	16.9%	105-115	8-11%
Pain	76.1	5.7%	80-95	2-5%
Autoimmune	47.5	16.8%	65-75	7-10%
Respiratory	38.5	4.8%	40-50	2-5%
Antibiotics & Vaccines	38.3	3.2%	40-48	1-4%
Cardiovascular	40.6	-1.8%	36-44	(-2)-1%
HIV	26.7	11.5%	32-40	5-8%
Mental Health	36.1	-2.6%	32-38	(-2)-1%
Antivirals	23.8	25.0%	16-20	(-7)-(-4%)
All Others	368.3	5.1%	445-460	3-6%

Source: IQVIA Therapy Prognosis, Sep 2017; IQVIA Institute, Oct 2017

Notes: Includes 8 Developed and 6 Pharmerging countries: U.S., France, Germany, Italy, Spain, United Kingdom, Japan, Canada, China, Brazil Russia, India, Turkey, Mexico; CAGR = Compound Annual Growth Rate

**Exhibit 28: Global Top 20 Countries Ranking and Index Relative to U.S.**

2012			2017			2022		
RANK	COUNTRY	INDEX	RANK	COUNTRY	INDEX	RANK	COUNTRY	INDEX
1	U.S.	100	1	U.S.	100	1	U.S.	100
2	 China	24	2	China	26	2	China	28
3	 Japan	24	3	Japan	18	3	Japan	13
4	Germany	11	4	Germany	10	4	Germany	9
5	 France	10	5	France	7	5	 Brazil	8
6	Italy	7	6	 Brazil	7	6	 France	6
7	 Brazil	6	7	 Italy	6	7	Italy	6
8	U.K.	6	8	U.K.	6	8	U.K.	5
9	 Spain	5	9	Spain	5	9	 India	5
10	 Canada	5	10	Canada	4	10	 Spain	4
11	 India	4	11	India	4	11	 Canada	4
12	 South Korea	3	12	 Russia	3	12	Russia	4
13	 Australia	3	13	 South Korea	3	13	South Korea	3
14	 Russia	3	14	 Australia	3	14	Australia	2
15	 Mexico	2	15	Mexico	2	15	 Turkey	2
16	 Argentina	2	16	 Turkey	2	16	 Mexico	2
17	 Saudi Arabia	2	17	 Poland	2	17	 Argentina	2
18	 Poland	2	18	 Saudi Arabia	1	18	 Poland	1
19	 Switzerland	2	19	 Argentina	1	19	 Saudi Arabia	1
20	 Belgium	2	20	 Switzerland	1	20	Switzerland	1

Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017

 Change in Ranking over Prior Five Years

# Appendix

**Exhibit 29: Global Spending and Growth in Selected Countries**

	2017 SPENDING US\$BN	2013-2017 CAGR CONSTANT US\$	2022 SPENDING US\$BN	2018-2022 CAGR CONSTANT US\$
<b>Global</b>	<b>1,135.1</b>	<b>6.2%</b>	<b>1,415-1,445</b>	<b>3-6%</b>
<b>Developed</b>	<b>753.2</b>	<b>5.8%</b>	<b>915-945</b>	<b>2-5%</b>
U.S.	466.6	7.3%	585-615	4-7%
EU5	154.4	4.4%	170-200	1-4%
Germany	45.1	4.9%	51-61	2-5%
France	33.1	1.3%	36-40	0-3%
Italy	29.0	5.5%	34-38	2-5%
U.K.	25.7	6.9%	29-33	2-5%
Spain	21.5	4.6%	24-28	1-4%
Japan	84.8	2.0%	85-89	(-3)-0%
Canada	20.7	3.9%	23-27	1-4%
South Korea	13.7	4.5%	15-19	3-6%
Australia	13.1	4.7%	12-16	1-4%
<b>Pharmerging</b>	<b>269.6</b>	<b>9.7%</b>	<b>345-375</b>	<b>6-9%</b>
China	122.6	9.4%	145-175	5-8%
Tier 2	67.3	11.2%	89-93	7-10%
Brazil	33.1	11.5%	38-42	5-8%
India	19.3	11.0%	26-30	9-12%
Russia	14.9	10.8%	20-24	7-10%
Tier 3	79.7	8.9%	95-125	6-9%
<b>Rest of World</b>	<b>112.3</b>	<b>2.0%</b>	<b>125-155</b>	<b>2-5%</b>

Source: IQVIA Market Prognosis, Oct 2017

Notes: CAGR = Compound Annual Growth Rate



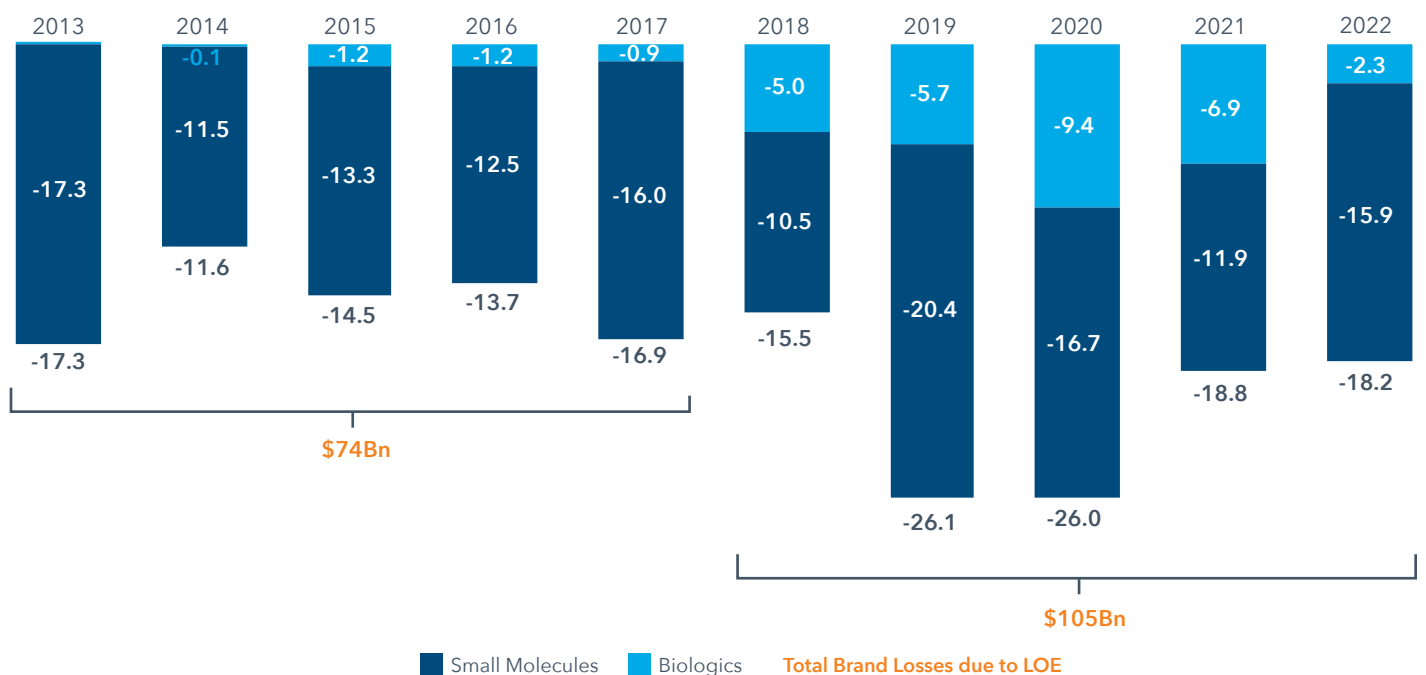
### Exhibit 30 : Global Medicine Spending Share and Growth by Region and Product Type

SPENDING 2022 US\$	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER PRODUCTS	TOTAL US\$BN
<b>Global</b>	44%	28%	13%	15%	1,415-1,445
Developed	64%	14%	14%	8%	915-945
Pharmerging	25%	40%	14%	22%	345-375
Rest of World	51%	27%	8%	14%	125-155

2018-2022 CAGR CONSTANT US\$	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER PRODUCTS	TOTAL GROWTH
<b>Global</b>	1-4%	4-7%	5-8%	4-7%	3-6%
Developed	(-1)-2%	2-5%	2-5%	0-3%	0-3%
Pharmerging	6-9%	5-8%	8-11%	5-8%	6-9%
Rest of World	1-4%	4-7%	2-5%	3-6%	2-5%

Source: IQVIA Market Prognosis, Oct 2017  
 Notes: CAGR = Compound Annual Growth Rate

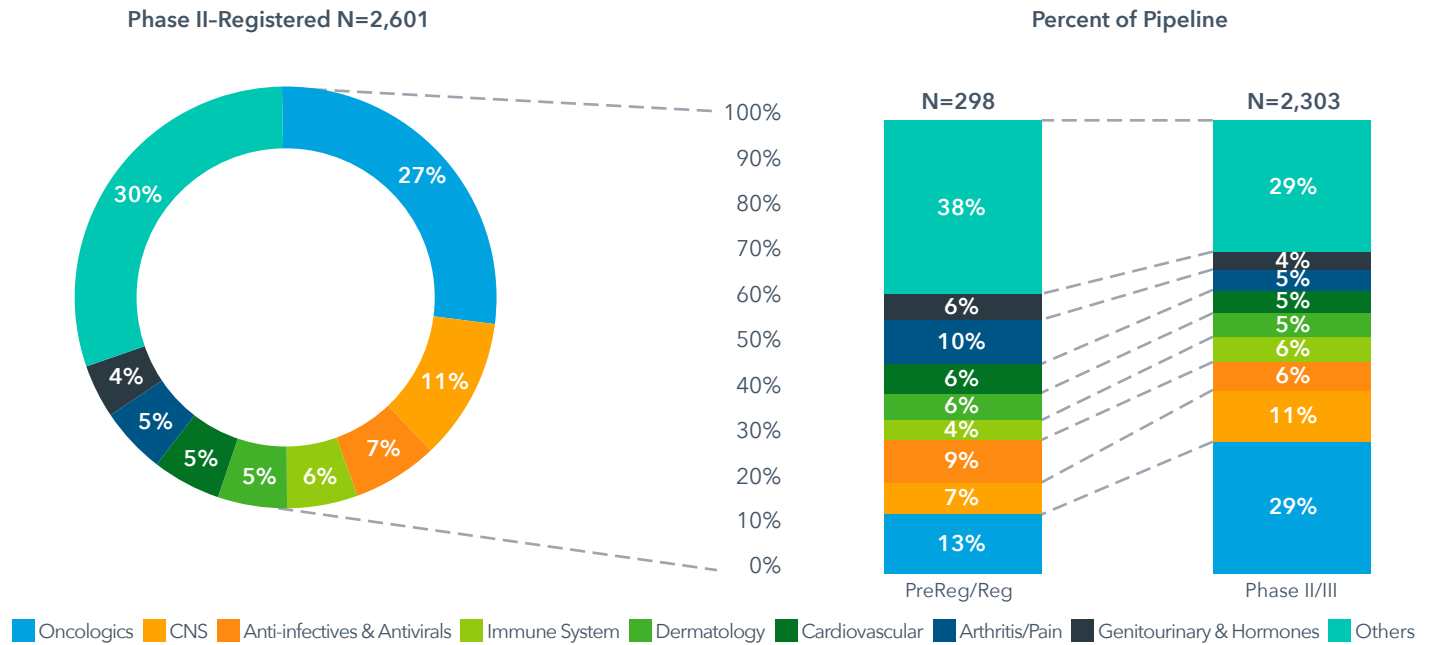
### Exhibit 31 : U.S. Impact of Brand Losses of Exclusivity 2013-2022, US\$Bn



Source: IQVIA Institute, Jan 2018

# Appendix

**Exhibit 32: Global Active R&D Pipeline Phase II to Registered**



Source: IQVIA Market Prognosis, Sep 2017; IQVIA Institute, Oct 2017

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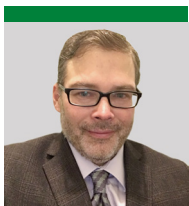
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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.



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# About the IQVIA Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including, including government agencies, academic institutions, the life sciences industry and payers.

## Research Agenda

The research agenda for the Institute centers on 5 areas considered vital to contributing to the advancement of human health globally:

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

## Guiding Principles

The Institute operates from a set of Guiding Principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.



The IMS Institute is now the  
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