State Medicaid Alternative Reimbursement and Purchasing Test for High-cost Drugs (SMART-D)

Economic Analysis

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Executive Summary

The recent introduction of a small number of expensive specialty drugs has drastically affected state Medicaid budgets. Medicaid expenditures on prescription drugs reached $42.3 billion in 2014—an increase of 14% in only one year—and new specialty drugs have been a significant factor in escalating overall program costs. Other factors contributing to the high amount of spending on prescription drugs are an increase in the number of participants enrolled in Medicaid and the high prevalence of disease in that population.

This SMART-D analysis investigates the current and likely future role of high-cost drugs in Medicaid expenditures. There is no standard definition of "high-cost," so the study team adopted its own two-part definition; high-cost drugs must meet both requirements:

- Reimbursements of more than $600 per prescription and
- Total Medicaid reimbursements of $72 million per year.

Using data from the Centers for Medicare and Medicaid Services (CMS) Medicaid Drug Utilization Database, the study team identified 64 drugs that meet both criteria. In FY 2015, these 64 drugs accounted for 1.5% of prescriptions and 32.6% of drug reimbursement dollars. Looking ahead, this report identifies 110 new drugs in the pipeline, many of which have the potential to significantly affect Medicaid budgets.

Goals of Phase 1 Economic Analysis

The Congressional Research Service has identified high-cost specialty drugs as a primary driver of spending growth in the U.S. healthcare system (CRS, 2015). These innovative therapies treat serious conditions such as cancer, hepatitis C, blood disorders, and HIV. But the cost of providing these therapies has had a dramatic and unforeseen impact on state Medicaid programs, which are tasked with providing these expensive drugs to a population with a high prevalence of chronic conditions while operating under fixed annual budgets.

This analysis will identify the ways in which high-cost prescription drug spending has affected state Medicaid programs. Specifically, the report provides this information:

- Documentation of the recent growth in Medicaid spending for drugs
- Definition of high-cost specialty drugs
- Estimation of Medicaid expenditures of recently released high-cost drugs
- Identification of potential high-cost specialty drugs in the pipeline

Overview of Medicaid Prescription Drug Spending

The Medicaid program covers nearly 70 million Americans (Kaiser, 2015a) and is the nation's primary public health insurer. Altogether, Medicaid finances 16% of total personal healthcare spending in the U.S. (Kaiser, 2015a). Spending depends on how many recipients are enrolled, what services are covered by state and federal policies, how often recipients utilize services, and how much providers are paid for those services. Federal law allows states some flexibility in designing and administering their Medicaid programs, with each program's financing divided between the state and the federal government (Kaiser, 2015a).

Between 2013 and 2014, the U.S. as a whole experienced a 12.2% increase in outpatient prescription drug costs, the largest increase in more than a decade. During this yearlong period, spending by Medicaid on prescription drugs increased even more rapidly—14% in overall costs and 3.6% in expense per enrollee (MACPAC, 2015), with total spending increasing from $37.1 billion to $42.3 billion. The Centers for Medicare and Medicaid Services (CMS) identified several drivers for the sudden growth in spending, including "increased spending for new medications (particularly for specialty drugs such as hepatitis C), a smaller impact from patent expirations, and brand-name drug price increases" (CMS, 2015).

Table 1. ***Historical Medicaid Program and Gross Prescription Drug Spending (FY 2010–2014)***

Fiscal year	Total spending (billions)	Rx spending (billions)	FY enrollment (millions)	Total spending per FY enrollee	Rx spending per FY enrollee	Annual growth		
						Total spending per enrollee	Rx spending per enrollee	Enrollment
2010	388.1	31.6	54.6	7,108.1	578.8	5.2%	0.0%	7.3%
2011	411.7	36.5	56.5	7,290.4	646.3	2.6%	11.7%	3.4%
2012	416.2	37.8	58.0	7,177.5	651.8	-1.5%	0.8%	2.7%
2013	432.4	37.1	58.9	7,342.5	629.9	2.3%	-3.4%	1.6%
2014	472.7	42.3	64.8	7,294.3	652.7	-0.7%	3.6%	10.0%

Note: Expenditures are in current dollars; FY=fiscal year; Rx=prescription drug
Source: MACPAC, CMS

State Medicaid budgets have been drastically affected by the introduction of a small number of expensive specialty drugs. In a recent 50-state budget survey, a majority of states identified specialty and other high-cost drugs as a major factor in increasing financial outlays. These high-cost therapies include hepatitis C antivirals, oncology drugs, cystic fibrosis agents, hemophilia factor drugs, and cholesterol medications (NCBI, 2015). The private sector has also been affected by higher costs. For Express Scripts, a national pharmacy benefit manager, specialty drug spending increased by a record 31% in 2014, and it is forecast to increase 21% to 22% annually for the next three years (Express Scripts, 2015). Specialty medications managed through the pharmacy benefit currently account for more than 32% of a health plan's total pharmacy

spending, but the specialty drug percentage could increase to nearly half of total pharmacy expenditures by 2019 (Express Scripts, 2015).

Increases in Medicaid prescription drug expenses are also due to a spike in prices and acquisition costs for certain kinds of generic drugs (Smith et al., 2015). Although the higher cost of generic drugs is seen as troubling, thus far the issue appears to be limited to small market segments. A recent Department of Health and Human Services report (DHHS, 2016) attributes the rising cost of generic drugs to markets in which there is little competition because barriers to enter the market are high, mergers and acquisitions of pharmaceuticals have eliminated competitors, or drug producers have exited the market and thus reduced competition. Still, the cost of generic drugs has remained small compared to brand-name drugs. In the Medicaid program, generic drugs accounted for 81% of prescriptions, but only 26% of expenditures (DHHS, 2016).

State Medicaid programs can pay directly for prescription drugs for some of their enrollees through fee-for-service delivery systems, but increasingly rely on capitated arrangements with managed care health plans. Of the almost 64.8 million people covered by Medicaid in 2014, 43 million were enrolled in some kind of managed care, up 24% from 2013 (CMS, 2014). In a Medicaid state budget survey in October 2015, representatives of 35 states indicated that they "carve-in" prescription drugs to some degree in their contracted managed care arrangements (Smith et. al., 2015). Almost 60% of Medicaid prescription drug costs ($14 billion) are covered through Medicaid managed care plans, according to the Medicaid and CHIP Payment and Access Commission (MACPAC). Managed care organizations rely more heavily on generic drugs, spending a higher proportion of drug costs on generic drugs (26%) than fee-for-service programs (20%) do.

Medicaid Population Disease Prevalence

Medicaid programs are especially affected by high-cost specialty drug expenditures because the population they cover has a greater prevalence of illness than the rest of the U.S. Medicaid enrollees generally include low-income individuals, pregnant women, children, elderly people who also receive Medicare coverage, and disabled individuals. For many enrollees with disabilities, Medicaid may provide lifelong health care coverage. Compared to the general population, Medicaid beneficiaries are more likely to be overweight, smoke cigarettes, and have some limitation in basic physical activity. In addition, they have a disproportionate number of chronic health conditions, such as hypertension, coronary heart disease, and diabetes (MACPAC, 2015). These factors contribute to a per capita cost for Medicaid beneficiaries that is more than $2,000 above that for the private insurance market (CMS, 2015).

Nearly 70% of Medicaid's resources are utilized by 30% of its enrollees. The majority of Medicaid spending is devoted to people with multiple chronic conditions. In addition, many of the highest-utilizing patients suffer from both chronic illness and disabilities (Kronick et al., 2007).

Table 2. ***Prevalence of Major Chronic Illness Categories in Medicaid for Disabled and Aged***

CDPS Category	Disabled	Aged	Disabled (Medicaid only)	Disabled (Dual Eligible)
Cardiovascular	31.5%	51.5%	28.4%	36.5%
Psychiatric	28.8%	10.4%	29.3%	28.0%
Central nervous system	21.9%	18.1%	22.7%	20.7%
Pulmonary	19.4%	19.6%	19.8%	18.8%
Skeletal and connective	19.0%	24.7%	17.6%	21.4%
Gastrointestinal	15.8%	5.0%	15.6%	16.0%
Diabetes	14.7%	19.9%	12.7%	18.0%
Renal	10.0%	12.9%	8.5%	12.6%
Skin	8.5%	9.3%	8.1%	9.1%
Developmental disability	7.0%	0.6%	6.5%	7.8%
Eye	6.7%	18.6%	5.0%	9.5%
Metabolic	6.0%	5.6%	6.7%	4.8%
Substance abuse	5.3%	0.7%	5.9%	4.3%
Infectious disease	4.2%	3.2%	4.4%	4.0%
Cancer	3.9%	6.9%	3.6%	4.3%
Cerebrovascular	3.7%	8.9%	3.1%	4.7%
Genital	2.6%	3.0%	2.6%	2.6%
Hematologic	2.5%	1.9%	2.8%	2.2%
Pregnancy	1.1%	0.1%	1.5%	0.6%
Total Occurrence	**4,760,879**	**2,346,976**	**2,952,443**	**1,808,436**

Note: CPDS is the Chronic Illness and Disability Payment System (CDPS) used by Medicaid programs as a diagnostic classification
Source: (CHCS, 2007)

These highest-cost Medicaid beneficiaries have a complex mix of comorbidities and a wide range of psychosocial needs (CHCS, 2007). For those with eight or more diagnoses, hypertension (65%) and diabetes (56%) are the most common co-occurring diagnoses (CHCS, 2007). Among persons with disabilities, the most frequent co-occurring conditions are hypertension (23%), diabetes (14%), and behavioral health disorders, such as affective psychoses (9%) and schizophrenia (9%). In addition, central nervous system disorders and infectious diseases (including HCV and HIV diseases) are more prevalent among individuals with disabilities (Kronick, R., et al., 2007).

Many patients over 65 who qualify for Medicare may also remain in the Medicaid system if they meet the low-income and disability requirements. Among elderly patients in the Medicaid system, diabetes and cancer are the more prevalent illnesses.

Impact of High-Cost Specialty Drugs on State Medicaid Costs

High-cost specialty drugs are typically used to treat complex, often rare diseases. Many of these medicines require complicated protocols such as ongoing assessments of therapeutic responses, complex patient or provider training, special handling by specialty pharmacies or individualized distribution networks, and ongoing monitoring of side effects. For example, a CVS Health analysis found that 8.7% of Sovaldi users discontinued the therapy before the treatment concluded compared to 2% in clinical trials. The study recommended that new strategies be employed to improve adherence and maintain appropriate use (CVS Health, 2014).

Because high-cost specialty drugs often exceed $25,000 per prescription, state Medicaid programs have spent billions of additional dollars on prescription drugs. A recent report on prescription drug spending indicated that these specialty drugs accounted for 0.9% of claims but resulted in 32% of total spending (before rebates) in 2014 (MACPAC, 2016). Between 2011 and 2014, prescription drug expenditures by Medicaid increased by 12.2%, with prescription drugs accounting for $42.3 billion of total spending before rebates (see Table 1). Looking ahead, there are more drugs in the pipeline that are likely to have similar budgetary effects.

In 2015, Avalere Health, a consulting firm, analyzed the potential impact to state and federal Medicaid programs of 10 breakthrough drugs currently in the pipeline by measuring the price and utilization, by payer, for each drug. Medicaid's share of total utilization ranged from 7% for a late-stage lung cancer therapy to 40% for a cystic fibrosis therapy. These differences stem mostly from the age profiles of qualified patients: Most late-stage lung cancer patients are old enough to qualify for Medicare, whereas cystic fibrosis patients tend to be younger because the disease usually begins early in life. Using prices benchmarked for products already on the market, Avalere projected the fiscal impact on Medicaid for the 10 breakthrough drugs to be $15.8 billion over the next decade. Under the current cost-sharing arrangements, state Medicaid programs would be responsible for $7.4 billion in new prescription spending in that period.

State Medicaid program officials have taken various approaches to mitigating the cost of new drugs and unexpected costs, which have included establishing clinical prior authorization requirements, standardizing clinical criteria across fee-for-service and managed care, and negotiating lower prices or more aggressive rebates. For additional details, see the Center's policy brief entitled *Medicaid and Specialty Drugs: Current Policy Options*.

Defining High-Cost Drugs

Comparing the impact of high-cost specialty drugs across various programs is problematic because there is not a common definition among federal and state agencies and commercial payers. Instead, different agencies and researchers have developed thresholds based on the type of expenditure data available. Examples of definitions of high-cost specialty drugs include the following:

- Medicare Part D: drugs that cost more than $600 per month (CMS, 2015).

- Medicaid and CHIP Payment and Access Commission (MACPAC): drugs that average more than $1,000 per claim (MACPAC, 2016).
- Government Accountability Office (GAO): drugs with more than $9,000 in annual beneficiary expenditures for a drug (GAO, 2015).
- Medicare Payment Advisory Commission (MEDPAC): No specific threshold but tracks prices for single-source brand drugs, which are drugs manufactured by a single company that have no generic substitute.

To help refine our understanding of high-cost drugs, the SMART-D study team also assessed Food and Drug Administration (FDA) "breakthrough therapies." These breakthrough therapies receive attention because the designation suggests that a drug in the pipeline is likely to later becoming a high-cost specialty drug. The study team reviewed previous Medicare and Medicaid analyses to identify breakthrough therapies using the FDA Safety and Innovation Act (FDASIA) definition:

- Intended alone or in combination with one or more other drugs to treat a serious or life-threatening disease or condition and
- [Has] preliminary clinical evidence [that] indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

If a drug is designated as a breakthrough therapy, the FDA expedites its development and review, providing a response to the drug manufacturer's submitted application within 60 calendar days of receipt (FDA, 2014). The breakthrough therapy designation is intended to ensure that therapies for serious conditions are approved and available to patients as soon as it can be concluded that the benefits justify the risks (FDA, 2014). Recent research shows that a majority of physicians incorrectly believe that strong evidence is required for a breakthrough designation when, in fact, the FDA requires only preliminary evidence (Kesselheim, 2016). The characteristics of a drug that qualifies for the breakthrough therapy designation, along with the recognition deriving from the designation, suggest that the drug will have a high price. If the disease treated is especially prevalent among Medicaid recipients, high costs to Medicaid would be expected.

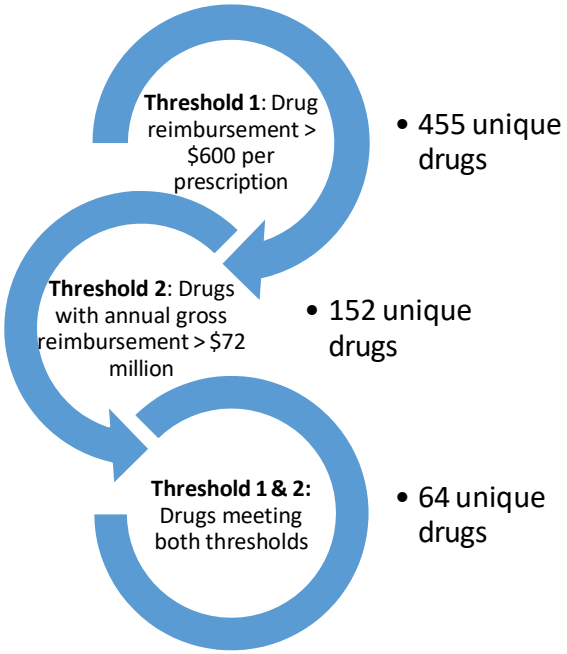
SMART-D definition of high-cost

For this project, the study team adopted a two-part definition that could be aligned with the available Medicaid data. The rationale for this approach is that price and utilization can independently affect total expenditures on prescription drugs. Thus, the study team attempted to identify and exclude from the analysis drugs that were either low-cost with high utilization or high-cost with very low utilization. These are the two requirements for a high-cost drug in this analysis:

- Reimbursements of more than $600 per prescription and
- Total Medicaid reimbursements of $72 million or more per year.

The first threshold requires an average total reimbursement (gross of rebates and including reimbursements from other sources) of more than $600 per prescription, analogous to the $600 per month threshold used by Medicare Part D. This per-prescription threshold eliminates drugs that are not expensive per prescription, but for which Medicaid reimburses a large number of prescriptions, such as insulin or albuterol.

The second threshold is at least $72 million in Medicaid reimbursement per year, gross of rebates, representing the cost to Medicaid of a $600-per-month drug used for one year by 10,000 Medicaid enrollees. It eliminates drugs with high costs per prescription but relatively low utilization. Examples of drugs that were excluded by the $72 million-per-year threshold include Metreleptin, Chenodiol, and several hemophilia blood-clotting factors.



After aggregating the CMS Medicaid State Drug Utilization Data across packaging, dosages, and labelers, there were 455 drugs for which average total reimbursements exceeded $600 per prescription and 152 drugs for which Medicaid reimbursements, gross of rebates, exceeded $72 million in the most recent four quarters for which data were available. There were 64 drugs that met both criteria. Appendix A lists those 64 drugs, their average total reimbursement per prescription, and their cost to Medicaid in FY 2015.

The 64 drugs categorized as high-cost drugs for this study accounted for 9.3 million prescriptions and $16.9 billion in Medicaid reimbursements, gross of rebates, or 1.5% of prescriptions reimbursed by Medicaid and 32.6% of Medicaid drug dollars. In FY 2015, the Medicaid program spent an estimated $538.4 billion (Kaiser, 2015b). The estimated $16.9 billion spent on these 64 high-cost drugs accounts for 3.1% of the total national Medicaid spending for all services.

Methods: Recent Spending on New High-cost Specialty Drugs

The study team used the most recent four quarters of Medicaid State Drug Utilization Data records (fourth quarter 2014 to third quarter 2015) to identify spending by Medicaid on drugs. The drugs were identified by the National Drug Code (NDC), which consists of universal product identifiers for drugs released under FDA approval. The codes contain 11 digits that can be used to identify every combination of labeler, product, and package size for available drugs.

To identify the costs of individual drugs, spending and numbers of prescriptions from utilization records were aggregated across packaging, dosages, and labelers by looking up the nonproprietary name for the drug in each record in the FDA's NDC database and combining records with the same name. The Medicaid State Drug Utilization Data used for this analysis include reimbursements for specialty drugs billed by physicians and pharmacies. The data contain prescriptions for Medicaid recipients enrolled in fee-for-service and managed-care programs. The utilization records also list the total reimbursement for the prescription, along with the portion that is Medicaid's responsibility. The difference between the two represents the member's share (if applicable by the state), as well as the portion that is the responsibility of other insurance such as Medicare or commercial insurance, or fees associated with Section 340B entities.

To identify the effects of new high-cost specialty drugs on Medicaid spending, the list of 64 high-cost drugs for FY 2015 was compared to the list of drugs reimbursed in 2012. Nine of the drugs that met the criteria for high cost in FY 2015 had no claims in 2012. Those nine drugs accounted for $3.2 billion in Medicaid reimbursement gross of rebates in FY 2015. Table 3. below lists these nine drugs.

Table 3. ***New High-cost Drugs Reimbursed by Medicaid (FY 2015)***

Brand Name	Breakthrough Therapy?	Primary Drug Indication	FY 2015 Total Reimbursement per Prescription	FY 2015 Gross Cost to Medicaid
Harvoni	Yes	Hepatitis C	28,300	1,540,228,000
Sovaldi	Yes	Hepatitis C	24,400	643,446,000
Novoseven	No	Hemophilia A or B	81,500	219,484,000
Tecfidera	No	Multiple sclerosis	5,300	199,262,000
Tivicay	No	HIV-1	1,400	166,653,000
H.P. Acthar	No	Lupus erythematosus	43,700	138,727,000
Triumeq	No	HIV-1	2,400	127,545,000
Viekira Pak	Yes	Hepatitis C	25,400	111,334,000
Olysio	No	Hepatitis C	19,900	73,568,000

Source: Medicaid State Drug Utilization Data records, FY 2014-2015

Of the nine new drugs on the high-cost drug list for FY 2015, three had been designated as breakthrough therapies: Sovaldi, Harvoni, and Viekira Pak. These three drugs accounted for $2.3 billion in Medicaid reimbursement gross of rebates in FY 2015. All three were in the range of $24,000 to $29,000 per prescription, gross of rebates.

Seventeen other drugs designated as breakthrough therapies were reimbursed by Medicaid in FY 2015. All of them cost more than $600 per prescription, but none exceeded $72 million in gross cost to Medicaid, partly because some entered the market late in FY 2015. Together, their gross cost to Medicaid totaled $235 million in FY 2015. Table 4 lists the designated breakthrough therapies reimbursed by Medicaid in FY 2015. All of the dollar amounts presented here are before rebates are factored in. The next section discusses how drug rebates are calculated in the Medicaid program.

Table 4. ***Designated Breakthrough Therapies Reimbursed by Medicaid (FY 2015)***

Brand Name	Breakthrough Therapy?	High-cost Drug?	FY 2015 Total Reimbursement per Prescription	FY 2015 Gross Cost to Medicaid
Harvoni	Yes	Yes	28,300	1,540,228,000
Sovaldi	Yes	Yes	24,400	643,446,000
Viekira Pak	Yes	Yes	25,400	111,334,000
Kalydeco	Yes	No	24,500	71,044,000
Rapamune	Yes	No	900	31,352,000
Imbruvica	Yes	No	9,200	22,223,000
Eylea	Yes	No	1,600	21,822,000
Ibrance	Yes	No	9,800	21,286,000
Lucentis	Yes	No	1,400	20,935,000
Promacta	Yes	No	5,900	20,347,000
Orkambi	Yes	No	20,000	9,629,000
Zykadia	Yes	No	11,400	3,544,000
Ofev	Yes	No	8,200	2,903,000
Esbriet	Yes	No	7,300	2,612,000
Opdivo	Yes	No	4,200	2,440,000
Zydelig	Yes	No	7,700	2,003,000
Keytruda	Yes	No	7,700	1,518,000
Gazyva	Yes	No	4,400	442,000
Technivie	Yes	No	23,400	258,000
Arzerra	Yes	No	8,500	185,000

Source: Medicaid State Drug Utilization Data records, FY 2014-2015

Rebate calculations

The Omnibus Budget Reconciliation Act of 1990 created the Medicaid Drug Rebate Program (MDRP) to ensure that Medicaid receives a net price that is consistent with the lowest or "best price" that manufacturers use to sell their drugs in public or private markets (MACPAC, 2015). In

exchange for the MDRP rebates, state Medicaid programs must allow reimbursement for all drugs in the rebate program. Under the MDRP rebate program, states can exclude coverage for drugs if the prescribed use is not for a medically accepted indication, or if the class of drugs is expressly excluded from coverage under Section 1927 of the Social Security Act. In addition, states can use levers like preferred drug lists, prior authorization, clinical coverage criteria, or quantity limits to manage their pharmacy programs.

The MDRP rebate is calculated using a formula defined in statute based on the average manufacturers' price (AMP). CMS calculates a unit rebate amount for each drug based on the established formula for that classification of drug, and then provides the unit rebate amount to each state quarterly (MACPAC, 2015). To calculate the rebate, state Medicaid programs multiply the unit rebate amount by the number of units reimbursed during the quarter. The states then submit an invoice and collect the MDRP rebates directly from the manufacturers. Because of the statutory definition, states receive the same MDRP rebate amount for each unit of a particular drug regardless of how much they pay the pharmacy or physician provider. Pharmacies or physicians can charge varying amounts for the drug, and therefore the *net* unit price (payment to the provider minus the rebate) can vary by state (MACPAC, 2015).

Under the current MDRP methodology, these are the basic rebate rates:

- 13% of the AMP for generic drugs
- 23.1% of the AMP for single-source and innovator multiple-source drugs
- 17.1% of the AMP for blood-clotting factors and exclusively pediatric drugs

For drugs other than generic drugs, the rebate amount can be increased above the basic rebate amount by either of two provisions:

- If the difference between the AMP and the best price, defined as the lowest price the manufacturer offers to any buyer (with exceptions, including the Veterans Administration), is greater than the basic rebate, then that difference becomes the rebate amount.
- If the manufacturer has increased the price of a drug faster than the inflation rate, a consumer price index penalty could apply. If the difference between the current AMP and what the AMP would be if it increased at the rate of inflation is greater than either the basic rebate or the best price rebate, that difference becomes the rebate amount.

Rebates and high-cost drugs

In most cases, new high-cost drugs are single-source or innovator multisource drugs, with an MDRP rebate amount of 23.1% of AMP. These are new drugs and have not been on the market long enough for inflation to be a factor, so it is unlikely that consumer price index penalties will apply. AMPs and best prices are not published, but in the case of a new high-cost drug it seems unlikely that the best price offered by the drug manufacturer will be better than the 23.1% rebate amount. The MDRP rebate amount therefore is likely to be 23.1% of AMP.

For calendar year 2014, CMS reports that MDRP rebates amounted to $18.9 billion, or 40.9% of gross reimbursements for all drugs. This 40.9% gross rebate amount is significantly higher than the 23.1% rebate for single-source or innovator multisource drugs. The study team believes that this higher overall rebate amount is driven by CPI penalties and best price discounts for drugs that are several years past FDA approval. It is therefore unlikely that a new, high-cost, single-source innovator drug would trigger a greater than 23.1% MDRP rebate because neither CPI penalties nor best price rules would apply.

In addition to the MDRP rebate, states can negotiate directly with drug manufacturers for supplemental rebates to further reduce expenditures, either individually or as a group that pools covered persons. Currently, 47 states have negotiated single or multistate supplemental rebate agreements with manufacturers (CMS, 2016). CMS reports for calendar year 2014 show that state-negotiated supplemental rebates amounted to $951 million, or 2.1% of gross reimbursements for all drugs.

Because states have strong incentives to negotiate for supplemental rebates on high-cost drugs, it is likely that supplemental rebates on new high-cost drugs will amount to a higher percentage of gross reimbursements. The study team expects, however, that the supplemental rebates will not be sufficiently higher (as a percentage) than the average to offset the lower (as a percentage) MDRP rebates on new high-cost drugs. Overall, the study team concludes that combined MDRP and supplemental rebates on new high-cost drugs are likely to amount to a lower percentage of gross reimbursements for those drugs than the average rebate percentage for all drugs.

Offsets to spending on preexisting drugs and other Medicaid spending

High-cost drugs for state Medicaid programs could play a role in offsetting other Medicaid spending, in that outpatient prescription drugs can complement medical procedures or replace some expensive ones (examples are transplants and inpatient hospitalizations). As new prescription drug therapies enter the market, they may eventually replace older drugs as the preferred treatment or standard of care if they are shown to be safer and more effective.

Given the high prevalence of chronic diseases in the Medicaid population, new drug therapies might be used as a tool for reducing Medicaid expenditures. In a 2015 report, Roebuck et al. analyzed data on 1.5 million Medicaid enrollees to determine that a 1% increase in prescription drug use for some chronic diseases could lead to marginal decreases in nondrug Medicaid costs. These results were similar to a 2012 Congressional Budget Office report, which found evidence that increasing the use of prescription drugs could offset costs elsewhere in the Medicare program.

If newer drugs are more effective or produce less severe side effects than previous iterations of drug therapy, this could offset other Medicaid expenditures for physician and hospital services and provide better overall outcomes. In addition, Medicaid spending might decrease if physician care in conjunction with newer prescription medications is more effective at managing chronic diseases. Although the introduction of high-cost and breakthrough drug therapies has had a

dramatic effect on state Medicaid budgets, there's evidence that those drugs could offset nondrug costs in Medicaid programs, particularly over the longer term. However, accurately quantifying these offsets and accounting for them within state budget cycles and constraints is challenging in the current payment scheme.

Challenges to State Medicaid Drug Analysis

A primary limitation of this analysis is measuring the role of rebates on total Medicaid spending. None of the federal publicly available sources for Medicaid drug data provide a complete picture of pharmacy utilization, spending, and rebates at the NDC level, a key component in understanding the true cost of drugs for state Medicaid programs. There are other challenges stemming from reliance on the Medicaid Drug Utilization Database as the foundation for the high-cost drug analysis. CMS developed the database for administrative functions, rather than policy research. Both data completeness and coverage are difficult to determine from the publicly available data. This makes it difficult to understand the direction and magnitude of error when generalizing expenditures to subpopulations in the Medicaid program.

Another challenge stems from the Affordable Care Act's low-income adult coverage expansion of Medicaid into two-thirds of American states, which began in 2014. The increase in enrollment contributed to an aggregate increase in Medicaid spending across service categories, which creates additional difficulties in isolating the effects of pharmaceutical pricing and utilization on Medicaid expenditure growth.

Future Pipeline Analysis and Implications

Drug development involves four broad phases: discovery, preclinical, clinical trials, and marketing (post-approval). The drug pipeline is a set of potential products that a manufacturer has under discovery or development at any given point in time. Generally, drug manufacturers have multiple compounds or products in their pipeline. Appendix B provides an overview of the pipeline as of mid-2016.

The U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) is responsible for ensuring that drugs available in the U.S. are safe and effective. Manufacturers test new drug molecules and submit relevant evidence through the new drug application process (FDA, 2016). A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the application (FDA, 2016). The Prescription Drug User Fee Act (PDUFA), enacted by Congress in 1992, authorizes the FDA to collect fees from drug companies, and these user fees have played an important role in expediting the drug approval process (FDA, 2016).

In 2015, CDER approved 45 novel drugs, the highest number since the creation of the PDUFA and well above the average of approximately 28 approvals per year from 2006 to 2014 (Diplomat, 2016). Of those approved in 2015, CDER identified 16 (36%) that were the first drug of their class, one indicator of the innovative nature of a therapy (Diplomat, 2016). Specialty drug products accounted for approximately half of the total new drugs and biologics approved by the FDA in

2015. Of the specialty agents that were new in 2015, the areas with the most approvals were rare diseases (25) and oncology (13). In the last five years, the FDA has favored more specialty medications than traditional ones for approval; thus, the impact of these generally high-cost medications continues to increase drug utilization and expenditures in the U.S. (Diplomat, 2016).

Special FDA designations—such as breakthrough, fast track, accelerated approval, and priority review—have been applied to promising drugs or those that treat diseases with an unmet medical need (FDA, 2014). These designations allow for expedited development through clinical trials and/or accelerated FDA review. Of the 45 novel drugs approved in 2015, 60% earned at least one of these special designations (Diplomat, 2016). Oncology represents the largest portion of the future pipeline, with approximately one dozen expected approvals for a variety of cancers (see Appendix B). Below is the number of new molecular entities (NMEs), a drug without precedent, that were most recently introduced for oncology.

- 41 NMEs approved in 2014 (~9 for oncology)
- 45 NMEs approved in 2015 (~13 for oncology)
- 13 NMEs approved thus far in 2016 (3 oncology)

The accelerating pace of drug innovation should be greeted as a welcome new frontier in improving health. Yet, this pace of innovation—and the accompanying uncertainty that real innovation brings—is challenging for Medicaid programs, state policy, and state budgets. Delivering patient access to new, effective therapies is the highest priority for state Medicaid leaders, who also must deliver on their legal and constitutional responsibilities to policymakers and taxpayers to operate within a fixed, balanced budget—a tension that Medicaid program leaders nationwide must manage.

Appendix A: High-cost drugs reimbursed by Medicaid (FY 2015)

Source: Medicaid State Drug Utilization Data records, 2014–2015

	Brand Name(s)	FY 2015 Total Reimbursement per Prescription[1]	FY 2015 Gross Cost to Medicaid	New Since 2012?
1	Abilify	900	2,746,712,000	NO
2	Harvoni	28,300	1,540,228,000	YES
3	Humira	3,500	693,300,000	NO
4	Truvada	1,400	667,395,000	NO
5	Sovaldi	24,400	643,446,000	YES
6	Atripla	2,200	596,965,000	NO
7	Latuda	800	555,665,000	NO
8	Omnitrope, Genotropin, Humatrope, Zomacton, Serostim, Saizen, Norditropin	3,500	485,258,000	NO
9	Invega	1,500	472,003,000	NO
10	Stribild	2,600	413,342,000	NO
11	Enbrel	3,000	396,948,000	NO
12	Prezista	1,200	336,474,000	NO
13	Complera	2,200	293,270,000	NO
14	Copaxone, Glatopa	5,300	276,151,000	NO
15	Advate	19,100	270,617,000	NO
16	Neulasta	3,600	248,221,000	NO
17	Reyataz	1,300	240,591,000	NO
18	Synagis	2,300	240,280,000	NO
19	Invega	1,000	221,648,000	NO

[1] Prescriptions are most commonly written for 30 days. In some circumstances, prescriptions can be 15, 60, or 90 days. The dataset used for this analysis does not provide data regarding days per prescription.

	Brand Name(s)	FY 2015 Total Reimbursement per Prescription[1]	FY 2015 Gross Cost to Medicaid	New Since 2012?
20	Novoseven	81,500	219,484,000	NO
21	Isentress	1,200	219,434,000	NO
22	Pulmozyme	3,300	202,733,000	NO
23	Tecfidera	5,300	199,262,000	YES
24	Vimpat	700	184,365,000	NO
25	Viread	900	183,553,000	NO
26	Gleevec	9,100	173,214,000	NO
27	Tivicay	1,400	166,653,000	YES
28	Remicade	3,500	150,666,000	NO
29	Herceptin	3,100	150,052,000	NO
30	Avastin	1,300	148,259,000	NO
31	Jadenu, Exjade	6,400	147,722,000	NO
32	Gammaplex, Flebogamma Dif, Vivaglobin, Gammagard, Bivigam, Privigen, Carimune, Gammagard S/D, Hizentra	3,100	146,327,000	NO
33	Kogenate Fs, Novoeight, Kovaltry, Nuwiq, Xyntha	21,500	142,953,000	NO
34	Creon, Ultresa, Viokace, Pertzye, Zenpep, Pancreaze	1,000	140,508,000	NO
35	H.P. Acthar	43,700	138,727,000	NO
36	Epzicom	1,200	137,677,000	NO
37	Onfi	900	135,133,000	NO
38	Revlimid	9,800	131,926,000	NO
39	Avonex,Rebif, Rebif Rebidose	5,200	131,275,000	NO
40	Triumeq	2,400	127,545,000	YES
41	Xolair	2,500	121,190,000	NO
42	Xifaxan	1,400	119,251,000	NO
43	Sabril	9,400	114,468,000	NO

	Brand Name(s)	FY 2015 Total Reimbursement per Prescription[1]	FY 2015 Gross Cost to Medicaid	New Since 2012?
44	Remodulin, Tyvaso, Orenitram	12,200	114,006,000	NO
45	Viekira Pak	25,400	111,334,000	YES
46	Zortress, Afinitor	7,900	104,599,000	NO
47	Rituxan	4,700	98,123,000	NO
48	Makena	2,700	97,899,000	NO
49	Eligard, Lupron Depot	1,800	94,554,000	NO
50	Implanon, Nexplanon	700	90,423,000	NO
51	Sprycel	8,800	89,670,000	NO
52	Gilenya	5,400	89,594,000	NO
53	Banzel	1,400	83,923,000	NO
54	Humate-P, Alphanate	21,800	83,737,000	NO
55	Feiba	50,100	83,540,000	NO
56	Cinryze, Berinert	32,300	80,357,000	NO
57	Xeloda	2,300	77,078,000	NO
58	Renvela	1,100	76,998,000	NO
59	Letairis	7,200	75,603,000	NO
60	Neupogen	1,300	75,602,000	NO
61	Stelara	11,700	75,180,000	NO
62	Olysio	19,900	73,568,000	YES
63	Saphris	600	72,472,000	NO
64	Renagel	1,300	72,398,000	NO

Appendix B: Pipeline Forecast

Cancer

Cancer vaccines are excluded from this section because they may be managed differently than prescription drug therapy and generally follow a different regulatory pathway.

Product Name	Description/Indication	Phase/Status	References
Rociletinib	EGFR mutation NSCLC—Seeking approval for the treatment of EGFR (with EGFR T790 mutation as detected by FDA- approved test) NSCLC previously treated with EGFR targeted therapy, ** Available information shows that this product has had mixed results in clinical trials. An FDA decision is expected in the near future, but it is unclear how effective the drug might be and whether it will gain approval.*	PDUFA = 6/28/2016 4/2016: FDA Advisory Committee voted 12 to 1 against granting accelerated approval. Committee recommended that the FDA wait for data from ongoing trial comparing this agent to chemotherapy.	http://www.reuters.com/article/us-clovis-oncology-fda-idUSKCN0X920A
Telotristat Etiprate		PDUFA = 11/30/16 for the treatment of carcinoid syndrome	http://www.lexpharma.com/pipeline/telotristat-etiprate.html
Apaziquone		PDUFA = 12/11/16 for the treatment of bladder cancer	http://www.businesswire.com/news/home/20160219005209/en/Spectrum-Pharmaceuticals-Announces-FDA%E2%80%99s-Acceptance-NDA-Filing

BTD: breakthrough therapy designation; BLA: biologic license application; NDA: new drug application; NSCLC: non-small cell lung cancer; Orphan Drug Status: status to a drug or biological product ("drug") to treat a rare disease or condition upon request of a sponsor; AML: acute myelogenous leukemia

Olaratumab	Exerts its effect by disrupting the platelet-derived growth factor (PDGF) receptor α pathway on tumor cells and on cells in the tumor microenvironment. Seeking approval in combination with doxorubicin for the treatment of people with advanced soft tissue sarcoma (STS) not amenable to curative treatment with radiotherapy or surgery.	5/2016: BLA accepted for priority review. Approval is possible before end of 2016.*	https://investor.lilly.com/releasedetail.cfm?ReleaseID=969023
Durvalumab [MEDI4736]	*Durvalumab is being tested in first-line bladder cancer as a monotherapy and in combination with tremelimumab as part of the DANUBE Phase III trial, which achieved first patient during the final quarter of 2015.*	BLA filing for the treatment of stage III. NSCLC is expected in 2017 and treatment for the third-line NSCLC is expected in the first half of 2016. A filing for the treatment of second line squamous cell carcinoma of the head and neck is expected in 2017. A filing for the treatment of first-line squamous cell carcinoma of the head and neck is expected in 2018. A filing for the treatment of first-line bladder cancer is expected in 2018. 2/17/16: granted BTD for the treatment of patients with PD-L1 positive inoperable or metastatic urothelial bladder cancer whose tumor has progressed during or after one standard platinum-based regimen.	

Acalabrutinib		Phase III for B-cell blood cancers. Estimated NDA submission before end of 2016.	https://www.astrazeneca.com/our-science/pipeline.html
VYXEOS™ (Cytarabine: Daunorubicin) Liposome for Injection [CPX-351]		Phase III for acute myeloid leukemia. Estimated NDA filing before end of 2016.	http://www.prnewswire.com/news-releases/celator-announces-phase-3-trial-for-vyxeos-cpx-351-in-patients-with-high-risk-acute-myeloid-leukemia-demonstrates-statistically-significant-improvement-in-overall-survival-300235620.html
Moxetumomab Pasudotox		Phase III for hairy cell leukemia. Estimated NDA submission in 2017.	https://www.astrazeneca.com/our-science/pipeline.html
Entinostat	*Available information indicates that this drug is in clinical trials combined with a number of other agents. Expected to be a significant approval, if approved.*	Phase III still recruiting for ovarian cancer.	http://www.pipelinereview.com/index.php/2016010560026/More-News/Merck-Pfizer-and-Syndax-Announce-Collaboration-to-Evaluate-Combination-of-Avelumab-and-Entinostat-in-Ovarian-Cancer.html http://lab.express-scripts.com/lab/insights/drug-options/2016-drug-pipeline-full-of-blockbuster-potential

Abemaciclib		Phase III 10/2015: Granted BTD for refractory hormone receptor positive (HR+) advanced or metastatic breast cancer.	https://investor.lilly.com/releasedetail.cfm?releaseid=935735
WhADI-PEG 20		Phase III	http://www.cbs8.com/story/32154522/polaris-group-reports-phase-iii-study-results-of-adi-peg-20-plus-best-supportive-care-in-advanced-hepatocellular-carcinoma
Aldoxorubicin		Phase III	http://www.pipelinereview.com/index.php/2014032453773/Small-Molecules/CytRx-Initiates-Pivotal-Global-Phase-3-Clinical-Trial-with-Aldoxorubicin-for-Second-Line-Treatment-of-Soft-Tissue-Sarcoma.html
Algenpantucel-L		Phase III	http://www.pipelinereview.com/index.php/2016051161164/Vaccines/NewLink-Genetics-Announces-Results-from-Phase-3-IMPRESS-Trial-of-Algenpantucel-L-for-Patients-with-Resected-Pancreatic-Cancer.html
Alisertib		Phase III for lung cancer. Development terminated for lymphoma.	

Apalutamide		Phase III for prostate cancer	http://adisinsight.springer.com/drugs/800032695
Avelumab		Phase II; information indicates possible accelerated approval.	http://www.pipelinereview.com/index.php/2016060661441/Antibodies/ASCO-2016-Pivotal-Avelumab-Study-Shows-Positive-Results-in-Metastatic-Merkel-Cell-Carcinoma.html
Bavituximab		Phase III for NSCLC. Development program is being redesigned. Granted BTD for the second-line treatment of NSCLC.	http://www.peregrineinc.com/pipeline/bavituximab-oncology.html
Binimetinib		Phase III	http://www.prnewswire.com/news-releases/array-biopharma-announces-phase-3-binimetinib-trial-meets-primary-endpoint-for-nras-mutant-melanoma-300193548.html
Brigatinib		Phase III	http://www.pipelinereview.com/index.php/2016060661450/Small-Molecules/ARIADs-Investigational-Medicine-Brigatinib-Demonstrates-54-%-Confirmed-Objective-Response-Rate-and-12.9-Month-Median-Progression-Free-Survival-in-ALTA-Study.html

Buparlisib		Phase III for breast cancer	http://www.ascopost.com/issues/january-25-2016/pi3k-inhibitor-buparlisib-extends-progression-free-survival-in-advanced-breast-cancer/ https://www.novartis.com/sites/www.novartis.com/files/2a_Pharmaceuticals_EN.pdf
Copanlisib		Phase III	http://www.prnewswire.com/news-releases/bayer-advances-clinical-development-program-for-investigational-cancer-drug-copanlisib-300065327.html
Custirsen		Phase III	http://www.pipelinereview.com/index.php/2015120259716/DNA-RNA-and-Cells/OncoGenex-Announces-Phase-3-AFFINITY-Trial-with-Custirsen-Continues-Following-Interim-Analyses.html
Duvelisib		Phase III for Non-Hodgkin's lymphoma and chronic lymphocytic leukemia	http://www.infi.com/home/research-development/pipeline/

Etirinotecan pegol		Phase III	http://www.pipelinereview.com/index.php/2016060161349/More-News/Nektar-Therapeutics-and-Daiichi-Sankyo-Europe-GmbH-Sign-European-Licensing-Agreement-for-ONZEALD-etirinotecan-pegol-an-Investigational-Drug-Candidate-Being-Developed-to-Treat-P.html
Encorafenib		Phase III for melanoma and colorectal cancer; expecting Phase III results in 2016.	http://www.arraybiopharma.com/product-pipeline/encorafenib-lgx818/
Eltrapuldencel-T		Phase III for melanoma	http://adisinsight.springer.com/drugs/800035277
Evofosfamide [TH-302]		Phase III. Did not achieve primary endpoint in recent Phase III trials; further development status unclear.	https://www.clinicaltrials.gov/study/NCT01746979?intr=Evofosfamide&aggFilters=phase:3&rank=1
Gilteritinib		Phase III for acute myeloid leukemia	http://newsroom.astellas.us/2015-10-28-Astellas-Inititaties-Phase-3-Registration-Trial-of-gilteritinib-ASP2215-in-Relapsed-or-Refractory-Acute-Myeloid-Leukemia-Patients http://www.astellasoncology.com/us/research-development.html

IMA901 (multiple tumor-associated peptides		Phase III	https://www.clinicaltrials.gov/study/NCT01265901?intr=IMA901&rank=2
Inotuzumab ozogamicin		Phase III 10/2015: received BTD for acute lymphoblastic leukemia.	http://www.pfizer.com/news/press-release/press-release-detail/pfizer_s_inotuzumab_ozogamicin_receives_fda_breakthrough_therapy_designation_for_acute_lymphoblastic_leukemia_all
Cositecan		Phase III for ovarian cancer	http://adisinsight.springer.com/drugs/800011000
Masitinib		Phase III for a wide range of cancers, inflammatory disease, and neurodegenerative disorders.	http://www.ab-science.com/en/human-medicine/masitinib-in-oncology
Midostaurin	2/2016: Granted BTD for newly diagnosed AML that are FLT3 mutation-positive.	Phase III; NDA submission planned for 2016.	https://www.novartis.com/news/media-releases/novartis-drug-pkc412-midostaurin-receives-breakthrough-therapy-designation-from-fda-newly-diagnosed-flt3-mutated-acute-myeloid-leukemia-aml
Momelotinib		Phase III for myelofibrosis	http://meetinglibrary.asco.org/content/148119-156

Motesanib		Phase III for NSCLC	http://www.pipelinereview.com/index.php/2015021756929/Small-Molecules/Takeda-Announces-Phase-3-MONET-A-Study-Evaluating-Motesanib-AMG-706-in-Patients-with-Advanced-Non-Squamous-Non-Small-Cell-Lung-Cancer-Does-Not-Meet-Primary-Endpoint.html
Multikine® leukocyte interleukin, injection		Phase III for head and neck cancer	http://www.cel-sci.com/cancer_multikine.html
Nelipepimut-S		Phase III for breast cancer	http://www.pipelinereview.com/index.php/2016041960988/Vaccines/Galena-Biopharma-Presents-GALE-301/GALE-302-Clinical-Booster-Data-at-the-American-Association-for-Cancer-Research-AACR-Annual-Meeting.html
Neratinib		Phase III for breast cancer	http://www.pipelinereview.com/index.php/2015092859086/Small-Molecules/Puma-Biotechnology-Announces-Presentation-of-Phase-III-Trial-of-PB272-in-Extended-Adjuvant-Breast-Cancer-ExteNET-Trial-in-Centrally-Confirmed-HER2-Positive-Early-Stage-Br.html

Pacritinib		2/2016: NDA for myelofibrosis withdrawn to reevaluate safety. Partial clinical hold placed on this product due to detrimental effects on survival.	http://www.prnewswire.com/news-releases/cti-biopharma-provides-update-on-clinical-hold-of-investigational-agent-pacritinib-and-new-drug-application-in-us-300217839.html
Plitidepsin		Phase III for multiple myeloma	https://www.pharmamar.com/2016/03/31/aplidin-shows-positive-results-in-pivotal-phase-iii-clinical-trial-for-multiple-myeloma/
Quizartinib		Phase III for relapsed and refractory acute myelogenous leukemia	http://www.daiichisankyo.com/rd/pipeline/development_pipeline/index.html
Rigosertib		Phase III for myelodysplastic syndrome	http://investor.onconova.com/releasedetail.cfm?ReleaseID=959595 http://www.onconova.com/product-pipeline/rigosertib.php
Rindopepimut		Phase III for glioblastoma	http://www.celldex.com/pipeline/rindopepimut.php
Rituximab biosimilar (Sandoz)		Phase III for follicular lymphoma	http://www.sandoz-biosimilars.com/en/aboutus/biosimilars-pipeline.shtml

Rucaparib	4/2015: granted BTD for monotherapy treatment of advanced ovarian cancer in patients who have received at least two lines of prior platinum-containing therapy, with BRCA-mutated tumors, inclusive of both germline BRCA and somatic BRCA.	Phase III for ovarian cancer	http://clovisoncology.com/products-companion-diagnostics/rucaparib/
Selumetinib	5/2016: granted Orphan Drug status for adjuvant treatment of patients with stage III or IV differentiated thyroid cancer.	Phase III for NSCLC and thyroid cancer. Estimated NDA filing in 2018.	https://www.astrazeneca.com/media-centre/press-releases/2016/selumetinib-granted-orphan-drug-designation-in-the-US-for-adjuvant-treatment-of-differentiated-thyroid-cancer-12052016.html https://www.astrazeneca.com/our-science/pipeline.html
Taselisib		Phase III for breast cancer	http://meetinglibrary.asco.org/content/147881-156
Talazoparib [BMN 673]	Also in development for the treatment of breast cancer (beyond gBRCA mutations), prostate cancer, small cell lung cancer, and ovarian cancer.	Phase III for BRCA-mutated breast cancer	http://www.pipelinereview.com/index.php/2015072058426/Small-Molecules/BioMarin-Provides-Program-Update-for-Talazoparib-in-Metastatic-Breast-Cancer.html http://www.medivation.com/research_developmen t/talazoparib
Tivantinib	2013: Granted Orphan Drug status for hepatocellular carcinoma.	Phase III for hepatocellular carcinoma	http://www.arqule.com/pipeline/tivantinib-arq-197/

Trebananib		Phase III	http://www.amgenoncology-international.com/%23/our-products/our-pipeline/
Tremelimumab	Available information indicated this drug is in development in combination with durvalumab.	Phase III	https://www.astrazeneca.com/our-science/pipeline.html
Veliparib		Phase III for NSCLC, breast cancer, and ovarian cancer	http://www.abbvie.com/research-innovation/pipeline.html
Volasertib		Phase III 9/2013: Granted BTD for acute myeloid leukemia.	https://www.boehringer-ingelheim.com/press-release/volasertib-fda-breakthrough-therapy-designation http://www.pipelinereview.com/index.php/2014091855463/Vaccines/Boehringer-Ingelheim-and-CureVac-announce-collaboration-to-develop-next-generation-lung-cancer-immunotherapy.html
Vosaraxin		Phase III	http://www.pipelinereview.com/index.php/2014100655631/Small-Molecules/Sunesis-Announces-Results-From-Pivotal-Phase-3-VALOR-Trial-of-Vosaroxin-and-Cytarabine-in-Patients-With-First-Relapsed-or-Refractory-Acute-Myeloid-Leukemia.html

Y-90 clivatuzumab tetraxetan		Phase III	http://www.pipelinereview.com/index.php/2016031560675/Antibodies/Immunomedics-Provides-Update-on-Phase-3-PANCRIT-1-Trial-of-Clivatuzumab-Tetraxetan-in-Patients-With-Advanced-Pancreatic-Cancer.html
Zastumotide		Phase III for melanoma	http://adisinsight.springer.com/drugs/800014109
Zoptarelin doxorubicin			http://www.pipelinereview.com/index.php/2015092859076/Proteins-and-Peptides/Aeterna-Zentaris-Zoptarelin-Doxorubicin-Meets-Phase-2-Primary-Endpoint-in-Men-with-Heavily-Pretreated-Castration-and-Taxane-Resistant-Prostate-Cancer.html

http://www.phrma.org/research/cancer
http://www.phrma.org/sites/default/files/pdf/2014-cancer-report.pdf
http://media.mmm-online.com/documents/176/the_pipeline_report_2016%E2%80%94big-t_43873.pdf

Immunology/Anti-Inflammatory

Agents in Development			
Product Name	**Description/Indication**	**Phase/Status**	**References**
RI-002	This product is a polyclonal formulation of Intravenous Immune Globulin, or IGIV, derived from human plasma containing naturally occurring polyclonal antibodies (e.g., Streptococcus pneumoniae. H. Influenza type B, Cytomegalovirus (CMV), measles, tetanus, etc.) and standardized, high levels of antibodies to respiratory syncytial virus (RSV).	PDUFA = 7/31/16 for the application for treatment of patients diagnosed with primary immune deficiency diseases.	http://www.admabiologics.com/drug-development/ri-002
ABP 501	Seeking approval for the treatment of plaque psoriasis and rheumatoid arthritis.* **This is a biosimilar for Humira®. If this agent can gain approval and clear the regulatory hurdles of becoming a biosimilar, it could be a significant approval. However, given various issues surrounding the cost and interchangeability of biosimilars, the real impact on cost remains unclear.*	PDUFA = 9/25/2016	http://www.rttnews.com/corpinfo/fdacalendar.aspx

Sarilumab		PDUFA = 10/30/2016 for treatment of active, moderate to severe RA.	http://www.rttnews.com/corpinfo/fdacalendar.aspx
Brodalumab		PDUFA = 11/16/16 for moderate to severe plaque psoriasis.	http://seekingalpha.com/news/3048846-fda-accepts-astrazenecas-brodalumab-bla-plaque-psoriasis-pdufa-date-november-16
Etanercept biosimilar (Sandoz)		10/2015: FDA accepts BLA for review. Seeking approval for all indications of reference product; approval in 2016 is possible.	https://www.novartis.com/news/media-releases/fda-accepts-sandoz-regulatory-submission-proposed-biosimilar-etanercept
Baricitinib	Inhibits the activity of the Janus (JAK) 1 and 2 enzymes	1/2016: BLA Accepted for review for the treatment of moderately to severely active RA. Approval before end of 2016 possible.	https://www.lilly.com/_Assets/SiteCollectionDocuments/Pipeline/Clinical-Development-Pipeline/index.html#PhaseIII
Daclizumab High-yield Process (Zinbryta™)		4/2015: BLA accepted for review. Approval in 2016 is possible.	http://www.msdiscovery.org/research-resources/drug-pipeline/548-daclizumab
Plecanatide	Chronic constipation	PDUFA = 1/29/17 for treatment of chronic constipation.	http://www.businesswire.com/news/home/20160419005404/en/Synergy-Pharmaceuticals-Announces-Acceptance-Drug-Application-Plecanatide
Ocrelizumab	2/2016: granted BTD for primary progressive MS.	Phase III for primary progressive MS. BLA expected in 2016	http://www.roche.com/investors/updates/inv-update-2016-02-17.htm

Sirukumab	RA	Phase III; BLA submission planned for 2016.	http://www.pmlive.com/pharma_news/gsk_plans_sirukumab_filing_in_rheumatoid_arthritis_next_year_890737
Tildrakizumab		Phase III for psoriasis; BLA submission in 2016/early 2017 possible.	http://www.sunpharma.com/Media/Press-Releases/Press-Release-Sun-Pharma-Announces-Positive-Results-of-Two-Pivotal-Clinical-Trials-of-Tildrakizumab.pdf
Masitinib		Phase III for a wide range of cancers, inflammatory disease, and neurodegenerative disorders.	http://www.ab-science.com/en/human-medicine/masitinib-in-oncology
Laquinimod		Phase III; Possible approval by 2018.	http://www.tevapharm.com/news/teva_and_active_biotech_announce_discontinuation_of_higher_doses_of_laquinimod_in_two_multiple_sclerosis_trials_01_16.aspx http://www.tevapharm.com/research_development/rd_focus/pipeline/
Ponesimod		Phase III for MS	
Ozanimod	Also in development for Crohn's disease and ulcerative colitis.	Phase III for MS	http://www.celgene.com/content/uploads/product-pipeline.pdf

Romosozumab		Phase III for osteoporosis	http://www.amgen.com/media/news-releases/2016/04/amgen-and-ucb-present-positive-data-at-endo-2016-comparing-romosozumab-with-teriparatide/
Alicaforsen		Phase III for IBD pouchitis	http://www.businesswire.com/news/home/20160211005502/en/Atlantic-Healthcare-starts-pivotal-Phase-3-trial
Rituximab biosimilar (Sandoz)		Phase III for RA	http://www.sandoz-biosimilars.com/en/aboutus/biosimilars-pipeline.shtml
Mongersen	Also in Phase II for ulcerative colitis.	Phase III for Crohn's disease	http://www.fiercebiotech.com/r-d/crohn-s-expert-flags-blockbuster-potential-and-frets-of-celgene-s-mongersen
Etrolizumab		Phase III for Crohn's disease and ulcerative colitis	http://www.etrostudiesresearch.com/etro-studies/
Anifrolumab	Systemic lupus erythematosus	Phase III; estimated BLA submission in 2019.	https://www.astrazeneca.com/our-science/pipeline.html
Odanacatib		Phase III for osteoporosis	http://www.merck.com/research/pipeline/home.html
Siponimod		Phase III for MS	http://www.msdiscovery.org/research-resources/drug-pipeline/7176-siponimod

Adalimumab biosimilar (Sandoz)		Phase III for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis and others	http://www.sandoz-biosimilars.com/en/aboutus/biosimilars-pipeline.shtml

BLA: biologic license application, IBS-C: irritable bowel syndrome, ITP: Idiopathic thrombocytopenic purpura, MS: multiple sclerosis, RA: rheumatoid arthritis

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http://media.mmm-online.com/documents/176/the_pipeline_report_2016%E2%80%94big-t_43873.pdf

Diabetes

Agents in Development			
Product Name	**Description/Indication**	**Phase/Status**	**References**
Lyxumia® (Lixisenatide)		PDUFA = 7/29/2016	http://www.biotechnologyevents.com/node/10587
LixiLan (insulin glargine and lixisenatide)		Manufacturer redeemed a Priority Review Voucher. FDA decision expected in 8/2016.	http://www.biotechnologyevents.com/node/10857
Xultophy (insulin degludec, liraglutide) - [previously known as IDegLira]		9/2015: NDA submitted. Approval mid- to late 2016 possible.	http://www.epgonline.org/news/novo-nordisk-files-nda-at-fda-for-xultophy-combination.cfm
Insulin Aspart faster-acting (NN1218)		12/2015: NDA submitted to FDA. Approval in mid to late 2016 possible.	http://www.novonordisk.com/content/Denmark/HQ/www-novonordisk-com/en_gb/home/media/news-details.1972083.html
Basaglar® (insulin glargine)	Long-acting insulin formulation for Type 1 and Type 2 Diabetes.	Launch planned for 12/2016	http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm477734.htm http://www.fiercepharma.com/legal/sanofi-patent-deal-lets-lilly-roll-out-a-lantus-biosim-u-s-next-december?utm_medium=nl&utm_source=internal

Exenatide extended-release [ITCA-650]	Implantable SC, continuous delivery formulation	Phase III; NDA submission planned for 3Q 2016 with possible approval mid to late 2017.	http://www.intarcia.com/pipeline-technology/itca-650.html
Semaglutide		Phase III; NDA submission possible late 2016/early to mid-2017. Oral formulation also in Phase II with Phase III expected to begin in 2016.	http://www.novonordisk.com/rnd/rd-pipeline.html
Saxagliptin + dapagliflozin		Initial application was denied in 10/2015 with a request for additional information. Estimate is that this drug is at least 6 months away from potential approval—ultimate date of market entry depends on what information the FDA requested and when the manufacturers resubmit it.	https://www.astrazeneca.com/media-centre/press-releases/2015/astrazeneca-receives-complete-response-letter-from-us-16102015.html
Omarigliptin		4/2016: plans to seek approval in US have been terminated.	http://www.mercknewsroom.com/news/company-statements/merck-provides-update-filing-plans-omarigliptin-investigational-dpp-4-inhibi
Evogliptin		Phase III	http://www.prnewswire.com/news-releases/tobira-therapeutics-and-dong-a-st-enter-into-license-agreements-for-evogliptin-and-cenicriviroc-300248967.html

Ertugliflozin		Phase III	http://www.mercknewsroom.com/news-release/research-and-development-news/merck-present-phase-3-data-investigational-medicines-ertu
Sotagliflozin		Phase III	http://www.lexpharma.com/pipeline/lx4211.html
Ertugliflozin + sitagliptin		Phase III	https://www.merck.com/research/pipeline/MerckPipeline.pdf
Canagliflozin + teneligliptin		Phase III	http://adisinsight.springer.com/drugs/800041134
Oral Semaglutide [O62175C]		Phase II	http://www.mmm-online.com/pipeline/the-pipeline-report-2016-big-time-upside/article/455119/4/
Retagliptin		Phase III in China. Development plan in US unclear at this time.	http://adisinsight.springer.com/drugs/800039203

NDA: new drug application

References:

http://www.phrma.org/sites/default/files/pdf/diabetes2014.pdf
http://lab.express-scripts.com/lab/insights/drug-options/2016-drug-pipeline-full-of-blockbuster-potential#sthash.UH5RiyzQ.dpuf
http://media.mmm-online.com/documents/176/the_pipeline_report_2016%E2%80%94big-t_43873.pdf

Behavioral Health

Agents in Development			
Product Name	**Description/Indication**	**Phase/Status**	**References/Where to Learn More**
Encenicline	Cognitive impairment in schizophrenia	Phase III; possible NDA submission in 2016, which could mean potential approval in mid to late 2017.	http://www.pipelinereview.com/index.php/2016032560770/Small-Molecules/FORUM-Pharmaceuticals-Inc.-Provides-Update-on-Encenicline-Phase-3-Clinical-Trial-Program-in-Cognitive-Impairment-in-Schizophrenia.html
Bitopertin	Schizophrenia	Phase III	http://www.pipelinereview.com/index.php/2014012153259/Small-Molecules/Roche-provides-update-on-the-first-two-of-six-phase-III-studies-of-bitopertin-in-schizophrenia.html
lofexidine	Relief of symptoms associated with acute opioid withdrawal	Phase III	http://www.usworldmeds.com/lofexidine.asp
RBP-7000 (dopamine-D2/serotonin-2 antagonist)	Schizophrenia	Phase III	http://www.pipelinereview.com/index.php/2015050557641/Small-Molecules/Indivior-PLC-Announces-Positive-Top-line-Results-From-Pivotal-Phase-3-Trial-of-RBP-7000-in-Schizophrenia.html

ALKS 5461 (buprenorphine/samidorp han)	Major depressive disorder	Phase III	http://www.forbes.com/sites/johnlamattina/2016/02/09/alkermes-ceo-richard-pops-on-alks-5461-and-challenges-in-developing-new-drugs-for-depression/#234d04b91a12

References:
http://www.phrma.org/sites/default/files/pdf/2014-mental-health-report.pdf
http://media.mmm-online.com/documents/176/the_pipeline_report_2016%E2%80%94big-t_43873.pdf

HIV

Agents in Development			
Product Name	**Description/Indication**	**Phase/Status**	**References/Where to Learn More**
Tenofovir Alafenamide		PDUFA = 11/12/2016	http://www.rttnews.com/corpinfo/fdacalendar.aspx
Ibalizumab (TMB-355)	Viral entry inhibitor Received BTD	Expected to complete BLA submission in 2016. Potential for approval in middle to second half of 2017.*	Which link goes here from below?
Fostemsavir	Virus attachment inhibitor Received BTD for patients having failed other treatment options	Phase III	http://adisinsight.springer.com/drugs/800031504 http://www.pharmatimes.com/news/us_breakthrough_for_bms_novel_hiv_drug_971691

BTD: breakthrough therapy designation

References:

https://www.poz.com/drug_charts/hiv-medications?utm_campaign=301_Redirect&utm_source=aidsmeds
http://www.phrma.org/sites/default/files/pdf/2014-meds-in-dev-hiv-aids.pdf
http://media.mmm-online.com/documents/176/the_pipeline_report_2016%E2%80%94big-t_43873.pdf

HCV

Agents in Development			
Product Name	**Description/Indication**	**Phase/Status**	**References/Where to Learn More**
Velpatasvir (GS-5816) + Sofosbuvir (GS-7977)	Sofosbuvir = nucleotide analog polymerase inhibitor velpatasvir = an investigational pan-genotypic NS5A inhibitor This agent is seeking approval in all genotypes of HCV. This could be what sets it apart from other available options.	PDUFA = 6/28/2016 (granted priority review)	http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3 http://www.fiercebiotech.com/biotech/gilead-announces-u-s-fda-priority-review-designation-for-sofosbuvir-velpatasvir-for?utm_medium=nl&utm_source=internal
Glecaprevir + Pibrentasvir [ABT-493 + ABT-590]	Glecaprevir [ABT-493] = NS3/4 protease inhibitor Pibrentasvir [ABT-590] = NS5A inhibitor	Phase III trials initiated in 2016. Estimated to gain approval in second half of 2017.	http://adisinsight.springer.com/drugs/800044162 http://www.datamonitorhealthcare.com/international-liver-congress-2016-glecaprevirpibrentasvir-will-pose-the-fiercest-competition-to-gilead-in-non-cirrhotic-patients/
Velpatasvir [GS-5816] + sofosbuvir [GS-7977] + voxilaprevir [GS-9857]	Sofosbuvir = nucleotide analog polymerase inhibitor velpatasvir = an investigational pan-genotypic NS5A inhibitor GS-9857 = NS3/4A protease inhibitor	Phase III; approval possible sometime in 2017.*	http://www.gilead.com/research/pipeline

Daclatasvir + Asunaprevir + beclabuvir [BMS-791325]	Daclatasvir = NS5A inhibitor Asunaprevir = NS3 protease inhibitor Beclabuvir = non-nucleoside Ns5B polymerase inhibitor	Phase III; approval possible sometime in 2017.*	http://www.pipelinereview.com/index.php/2014112756175/Small-Molecules/Bristol-Myers-Squibb-Receives-Complete-Response-Letter-from-U.S.-Food-and-Drug-Administration-for-Daclatasvir-an-Investigational-Treatment-for-Hepatitis-C.html
Grazoprevir + elbasvir + MK-3682 [MK-5172+MK-8742 + MK-3682]	Grazoprevir = NS3/4A protease inhibitor Elbasvir = NS5A replication complex inhibitor MK-3682 = NS5B inhibitor	Phase II - Phase III might begin in 2016 - it's possible you should see an NDA submission in 2017/2018	http://www.merck.com/research/pipeline/home.html

BTD: breakthrough therapy designation, HCV: hepatitis C virus
Reference: *https://www.hepmag.com/article/2016-hepatitis-c-treatment-research-pipeline*

Other

Abuse-deterring Opioids

- ER Hydrocodone by Teva - PDUFA = 6/7/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
  - http://www.tevapharm.com/news/teva_announces_fda_acceptance_for_review_of_nda_for_its_investigational_twice_daily_hydrocodone_bita rtrate_extended_release_tablets_with_proprietary_abuse_deterrence_technology_02_15.aspx
- ALO-02 (ER oxycodone/naltrexone) - PDUFA = 6/8/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
  - http://www.pfizer.com/news/press-release/press-release-detail/pfizer_announces_fda_acceptance_for_review_of_a_new_drug_application_fo r_alo_02_oxycodone_hydrochloride_and_naltrexone_hydrochloride
- KP201/APAP (IR hydrocodone/APAP) - PDUFA = 6/9/2016
  - https://globenewswire.com/news-release/2016/02/10/809381/0/en/FDA-Grants-Priority-Review-to-KemPharm-for-KP201-APAP-NDA.html
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
- SequestOX (oxycodone/naltrexone) - PDUFA = 7/14/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
  - http://www.biocentury.com/products/eli-200
- Remoxy (ER oxycodone) - PDUFA = 9/25/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
  - http://www.durect.com/products/development/remoxy/
- Arymo ER (ER morphine sulfate) - PDUFA = 10/14/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
  - http://www.prnewswire.com/news-releases/egalet-announces-fda-acceptance-of-new-drug-application-for-arymo-er-morphine-sulfate-extende d-release-tablets-300227415.html

Opioid Induced Constipation

- Oral Relistor® (methylnaltrexone bromide) - PDUFA = 7/19/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=2

Cardiovascular

- Bococizumab—Phase III for the treatment of hyperlipidemia
  - http://www.pfizer.com/sites/default/files/product-pipeline/Produce_Pipeline_Update.pdf
- Once monthly Repatha® (evolocumab) - PCSK-9 inhibitor for lipid lowering
  - PDUFA = 7/10/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=3
- Andexanet alfa—seeking approval for use as a reversal agent for factor Xa inhibitors
  - PDUFA = 8/17/2016
  - http://www.rttnews.com/CorpInfo/FDACalendar.aspx?PageNum=2
- Yosprala (enteric coated aspirin/omeprazole) for the secondary prevention of heart attack or stroke in patients at risk of aspirin-associated ulcers
  - PDUFA = 9/14/16
  - http://aralez.com/portfolio/yosprala/

Migraine Prevention

These agents should not be ignored—they might enter the market in late 2017 or early/mid 2018 (rough estimate). The drugs are injectable monoclonal antibodies and are likely to be quite costly.

http://www.empr.com/medical-news/new-novel-treatments-show-promise-for-migraine/article/343969/?DCMP=EMC-MPR_WeeklyNewsbrief&CPN=mylan_201 4&spMailingID=8452333&spUserID=NTEyNzc2NjI3NjMS1&spJobID=282652073&spReportId=MjgyNjUyMDczS0

- Calcitonin gene-related peptides (CGRPs)
  - AMG-334 - Phase III for prevention of episodic migraine
    - http://www.amgenpipeline.com/pipeline/
  - ALD403 - Phase III for prevention of episodic migraine
    - https://www.clinicaltrials.gov/study/NCT02559895?term=NCT02559895&rank=1
  - Galcanezumab [LY2951742] - Phase III for cluster headache (granted breakthrough therapy designation) and for prevention of migraine
    - https://investor.lilly.com/releasedetail.cfm?releaseid=918405
    - https://www.lilly.com/_Assets/SiteCollectionDocuments/Pipeline/Clinical-Development-Pipeline/index.html#PhaseIII
  - TEV-48125 - Phase III for prevention of chronic and episodic migraine
    - http://www.tevapharm.com/research_development/rd_focus/pipeline/

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