At OptumRx, our responsibility is to help ensure members have access to appropriate and cost-effective medications that are designed to improve health outcomes and lower overall medical costs. This is especially true during challenging times, such as the currently evolving COVID-19 situation. We remain steadfastly committed to providing our clients, members and the broader healthcare community with up-to-date information and support pertaining to drug access, cost management and notable FDA approvals.

As noted in the Q1 2020 issue of this report, we expect the emphasis on orphan drugs to continue this year, making up nearly 40% of newly approved drugs across all disease categories. Orphan drugs, or pharmaceuticals developed solely for the treatment of orphan diseases, are commercially underdeveloped due to the fact they are often not profitable to produce. What is new is that we now are starting to see the development of orphan drugs become more competitive, increasing the potential for reduced costs and broader patient accessibility.

In this report, we identify several significant drugs in the pipeline that either have just been approved or are expected to be approved by the FDA in the months ahead. In addition, we review a few critical larger trends to watch this year.

This OptumRx publication is designed to increase your understanding of the pharmaceutical pipeline for 2020.
Viltolarsen is in development to treat specific forms of Duchenne muscular dystrophy (DMD). DMD is a rare genetic disorder that affects young boys. DMD is characterized by progressive muscle deterioration and weakness. The onset of symptoms occurs between three and five years of age and worsens over time. Progressive muscle weakness leads to confinement to a wheelchair by the early teen age years. Later, patients experience life-threatening heart and respiratory conditions, with death commonly occurring in the late teens or twenties.

There is a significant unmet need for treatments for DMD, since it is associated with substantial sickness and death. DMD affects approximately 6,000 males in the U.S.

DMD is caused by a genetic mutation that results in the absence of a key protein called dystrophin that helps keep muscle cells intact. Viltolarsen “short circuits” the mutated genetic sequences through a process called “exon skipping.” Exon skipping allows the body to produce a dystrophin protein that is shorter than normal, but potentially still usable, for improved muscle function.

We have chosen three drugs that were recently approved or are nearing their anticipated approval dates in 2020 that could have a significant impact on payers and patients:

**risdiplam**

If approved, risdiplam would be the first oral therapy to treat spinal muscular atrophy (SMA). SMA is a rare group of severe neuromuscular disorders that lead to progressive muscle weakness and atrophy. Depending on the type of SMA, an individual’s physical strength and their ability to walk, eat or breathe can be significantly diminished or lost. It is the most common genetic cause of infant mortality and one of the most common rare diseases, affecting approximately one in 11,000 babies.

There is an unmet need for treatments for SMA, and especially for an all-oral option. There are currently only two FDA-approved drugs for SMA. Spinraza® (nusinersen) requires repeated, invasive injections into the cerebrospinal fluid in the spinal cord. The other alternative is Zolgensma® (onasemnogene abeparvovec), which is a one-time IV-infused gene therapy. In contrast, risdiplam is administered orally once daily.

Risdiplam is a gene-splicing intervention designed to correct a genetic defect which results in a reduction of the survival motor neuron 1 (SMN1), which leads to the weakness and disability of SMA. The drug helps the body produce more of the functional SMN protein and avoid the loss of these neurons.

While clinical trials are still ongoing, the early results for risdiplam are promising. However, we are lacking long-term efficacy and safety data, and it is unknown whether patients will achieve improved outcomes if risdiplam is used with or after other SMA therapies.

Competitively, risdiplam will be a relatively late market entry, with an expected FDA decision on or before August 24, 2020. Spinraza has been available since late 2016 and Zolgensma was approved in May 2019. While Spinraza does require invasive spinal injections, it has been widely used in SMA patients since its market entry. Practically speaking, the competitive advantage for risdiplam will rest mainly in its oral route of administration, and perhaps, a lower cost. For reference, the wholesale acquisition cost, (WAC), for a one-time dose of Zolgensma is approximately $2.1 million and Spinraza is approximately $750,000 in year one and $375,000 annually thereafter. However, the manufacturer has indicated that it will place a lower price on risdiplam.

**viltolarsen**

Viltolarsen is in development to treat specific forms of Duchenne muscular dystrophy (DMD). DMD is a rare genetic disorder that affects young boys. DMD is characterized by progressive muscle deterioration and weakness. The onset of symptoms occurs between three and five years of age and worsens over time. Progressive muscle weakness leads to confinement to a wheelchair by the early teen age years. Later, patients experience life-threatening heart and respiratory conditions, with death commonly occurring in the late teens or twenties.

There is a significant unmet need for treatments for DMD since it is associated with substantial sickness and death. DMD affects approximately 6,000 males in the U.S.
Drug Overview

We have chosen three drugs that were recently approved or are nearing their anticipated approval dates in 2020 that could have a significant impact on payers and patients (cont.):

**viltolarsen (cont.)**
If approved, viltolarsen would be the third exon-skipping drug for DMD, and the second specifically for the 8% of patients with a specific mutation. Vyondys 53™ (golodirsen) is also approved for this mutation, but there is limited efficacy data and unknown clinical benefit with its use.²

Data for viltolarsen are only available from early stage unpublished trials with small sample sizes. The FDA submission is based on data demonstrating an improvement in dystrophin levels, however there is disagreement among experts about exactly how much additional dystrophin might have a clinical benefit in patients with DMD. To date, very little safety data has been released.²

For reference, the average WAC price for Vyondys 53 is approximately $300,000 per year, but the cost varies significantly due to weight-based dosing.¹ The FDA is expected to make a decision in the 3rd quarter 2020.³

**Trodelvy™ (sacituzumab govitecan-hziy)**
An FDA decision for Trodelvy was made earlier than anticipated; it was approved on April 22, 2020.³

Trodelvy was approved to treat adult patients with metastatic triple-negative breast cancer (TNBC) who have received at least two prior therapies for metastatic disease. TNBC is an aggressive breast cancer that accounts for up to 20% of all breast cancer cases.

The term “triple negative” in TNBC means that this cancer tests negative for the three most common cancer causes – estrogen receptors, progesterone receptors and human epidermal growth factor receptor 2 protein (HER2). Therefore, TNBC does not respond to hormonal therapy medicines or medicines that target HER2.⁴ However, TNBC does respond to traditional chemotherapy.

Trodelvy is a novel antibody-drug conjugate (ADC), which combines both biologically engineered antibodies and traditional chemotherapy drugs (see below for more on ADCs). It is administered intravenously on a weekly basis over a 21-day cycle.⁵

One small published trial (108 patients) showed a 33% efficacy rate in a heavily pretreated population of patients with mTNBC.⁵ The most relevant adverse events (low white blood cell count and diarrhea), were managed with routine supportive care.⁵,⁶ Few patients discontinued treatment because of adverse events.⁵ Trodelvy is the first ADC targeted therapy for TNBC. There is a high unmet need for treatments in this subtype of breast cancer because of the size of the overall breast cancer population and the aggressive nature of TNBC.⁵ Industry analysts estimate that Trodelvy could reach $1.44 billion in 2024 global sales, initially as a third-line treatment for late-stage TNBC, although this drug is also being evaluated in earlier settings and other cancers as well.⁷
As mentioned above, Trodelvy is an antibody-drug conjugate (ADC) and these are a category of products to continue to watch in the drug pipeline.

To date, ADCs like Trodelvy have been an interesting combination of therapy monoclonal antibody plus extremely powerful small-molecule anticancer treatments. But the next generation of conjugates may branch into non-oncology indications, which could bring important benefits for a wide variety of unmet therapeutic needs.

Here is a quick look at these unique compounds:

- ADCs begin with engineered versions of the natural antibodies that are part of our immune system called monoclonal antibodies. These artificial antibodies have cancer-fighting features of their own, and are sometimes used as stand-alone cancer treatments. Yet monoclonal antibodies by themselves may not be enough to defeat some types of cancer.

- An ADC is formulated by joining (‘conjugating’) a potent small-molecule chemotherapy payload to the engineered antibody. Because they are based on natural immune cells, monoclonal antibodies can precisely discriminate between healthy and cancerous tissues.

Here is a simplified illustration of the main components of an ADC:
Precision targeting allows ADCs to deliver chemotherapy drugs that would otherwise be much too powerful to use on a stand-alone basis. How powerful? The chemical payload used in sacituzumab govitecan is **100 to 1,000 times more toxic** than traditional anticancer agents. But precision-guided ADCs can be highly lethal to the targeted cancer cells, while leaving healthy cells unharmed.

We can think of ADCs as a refinement or extension of precision medicine, which aims at maximizing therapeutic benefits while minimizing undesired side effects for an individual patient. As the field advances, we can look for new conjugate “payloads” that will go far beyond hunting cancer cells. Various manufacturers are exploring how to leverage the ADC approach to produce vaccines, radiological treatments, immunosuppressive, cardiovascular and more.

In addition to the eight ADC drugs approved by the FDA since 2010, there are nearly 100 investigational ADCs currently in pre-clinical and clinical trials for more than 35 different types of cancers in nearly 20 organs and tissues.

One recent paper sums-up the field this way: “Overall, the rise of non-oncology ADC therapeutics offers a huge opportunity for innovation at multiple fronts of drug discovery and development for years to come.”

### References


About OptumRx
OptumRx is a pharmacy care services company helping clients and more than 56 million members achieve better health outcomes and lower overall costs through innovative prescription drug benefit services, including network claims processing, clinical programs, formulary management, specialty pharmacy care and infusion services. Through expertise, flexible technology and a network of over 67,000 community pharmacies and state-of-the-art home delivery pharmacies, OptumRx is putting patients at the center of the pharmacy experience and making health care more connected and less fragmented — ensuring patients get the right medication at the right time at the best cost. OptumRx is part of Optum®, a leading information and technology-enabled health services business dedicated to making the health system work better for everyone. For more information, visit optum.com/optumrx or follow @OptumRx on Twitter.