Pipeline Preview 2020

Breakthrough Therapies for a Range of Conditions
While the number of drugs in development is rising, what is more impressive than the sheer number of candidates — and approvals — is the kinds of drugs being approved. Breakthrough Therapies, in particular, are once again making up a significant portion of new drugs coming to market — up from 20 percent of approvals in 2015 to 41 percent in 2017. The number dropped to 23 percent in 2018, a year with a record number of approvals. Such therapies can provide important options for patients with previously untreatable conditions or for whom other modes of action failed — and pose important cost considerations for payors.

Here’s an early look at some key Breakthrough Therapies expected to be reviewed by the U.S. Food and Drug Administration (FDA) in 2020.

NASH: Obeticholic Acid

Non-alcoholic steatohepatitis (NASH), is a severe form of fatty liver disease that is marked by inflammation and damage to liver cells — and in the most serious cases advanced fibrosis, cirrhosis, liver failure or liver cancer. The National Institutes of Health estimates that 3 to 12 percent of U.S. adults have NASH, and almost 40 percent of those with NASH have some level of fibrosis.

This fall, Intercept Pharmaceuticals filed a New Drug Application for obeticholic acid (OCA) to treat fibrosis in patients with NASH. OCA targets the farnesoid X receptor, which plays a key role in regulating metabolism of fats and glucose, as well as liver inflammation and liver cancer. The drug has been designated as a Breakthrough Therapy, and if approved will be the first drug specifically for NASH, though several other agents are currently in development. Currently, vitamin E and pioglitazone are used off-label as treatments for NASH.

In Phase III trials, 23.1 percent of patients on a high-dose of OCA showed improvement in fibrosis with no worsening of NASH after 18 months, compared to 11.9 percent of the placebo group. OCA is already the active ingredient of Ocaliva, approved in 2016 for the treatment of primary biliary cholangitis, a rare chronic liver disease. In that orphan indication, the drug is priced at about $70,000 a year. But there is speculation that Intercept will set a lower price for the NASH product. An FDA decision is expected by May 2020. If approved, OCA will likely be covered under the pharmacy benefit.

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Non-Hodgkin’s Lymphoma: Lisocabtagene Maraleucel

One potentially promising avenue for cancer treatment is the use of chimeric antigen receptor T-cell therapies (CAR T-cell), in which T-cells (the immune system’s hunter-killers) are removed from the patient’s body, genetically engineered to target a specific cancer, and then reinjected.\textsuperscript{13} Two CAR T-cell therapies have already been approved for certain kinds of non-Hodgkin’s lymphoma: Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel).\textsuperscript{14,15} Yescarta is also approved for relapsed or refractory acute lymphoblastic leukemia.

They may be joined in 2020 by a third CAR T-cell therapy for lymphoma: Celgene’s lisocabtagene maraleucel (liso-cel) for the treatment of relapsed or refractory B-cell non-Hodgkin’s lymphoma, including diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, and follicular lymphoma.\textsuperscript{16} In a Phase III trial, patients treated with the pivotal dose, had an overall response rate at 6 months of 49 percent and a complete response rate of 46 percent.\textsuperscript{17}

Liso-cel is expected to have a price tag similar to that of Yescarta and Kymriah — $400,000 for a one-time dose. If approved, lisocabtagene maraleucel will likely be covered under the medical benefit.\textsuperscript{18}

Hemophilia Gene Therapy: Valoctocogene Roxaparvovec

It’s estimated that more than 20 cell- and gene-based treatments will come up for, or receive, FDA approval over the next year and a half.\textsuperscript{19} These therapies offer immense potential benefits to patients — in some cases offering cures to life-threatening diseases in a single dose. But with their extremely high costs, combined with uncertainties over the permanence of their effects, they present challenges for payors.\textsuperscript{20}

One particularly significant gene therapy candidate is BioMarin’s valoctocogene roxaparvovec, a therapy for severe hemophilia A in patients aged 18 and older, which is expected to be approved sometime between the second and late third quarter of 2020.\textsuperscript{21}

Hemophilia A occurs about once per 5,000 live male births, with an overall U.S. prevalence of about 16,000.\textsuperscript{22} Severe hemophilia (<1 percent of normal factor VIII levels) accounts for about 60 percent of cases. The disease occurs when the gene responsible for producing clotting factor VIII is mutated, causing the body to produce inadequate levels of factor VIII, disrupting clotting and leading to bleeding episodes. Hemophilia A is typically treated with infusions of the missing clotting factor, though about one-third of patients ultimately develop resistance to therapy.\textsuperscript{23} BioMarin’s gene therapy, a one-time injection, uses a viral vector, to deliver a functional copy of the gene to the patient’s cells.\textsuperscript{24}

In preliminary data from a Phase III trial, 16 patients in the high-dose cohort had an annualized bleed rate reduction of 85 percent from baseline and their use of factor VIII fell by an annualized rate of 94 percent.\textsuperscript{25} Recently, based on three years of data from Phase I/II trials, BioMarin predicted that the effects of treatment would last for up to eight years.

The company plans to file for approval in the United States and Europe in the fourth quarter of 2019, and the drug could be available as early as mid-2020.\textsuperscript{26,27} Pricing has not been set, but current prices for gene therapies have ranged upward of hundreds of thousands of dollars.
Peanut Allergy: Palforzia and Viaskin Peanut

Peanut allergy is the most common of childhood food allergies.

Currently, there are no FDA-approved treatments for peanut allergy and it is commonly managed with rescue epinephrine.

Two new products in the market could be the beginning of what is expected to be a $4.5 billion global market in the category. These new treatments are aimed at building up a level of tolerance, which can help prevent a fatal allergic reaction due to accidental exposure.

The first drug likely to come to market is Aimmune’s Palforzia, which is pending approval for use to reduce the incidence and severity of allergic reactions after accidental exposure to peanut in patients aged 4 to 17 years, expected to be approved in January 2020. It is not a drug in a traditional sense but defatted, carefully measured doses of peanut flour that are administered orally to patients over a period of months. Dosing starts at half a milligram and builds up over six months to 300 milligrams — roughly the protein content of a single peanut — after which patients continue to receive maintenance doses of Palforzia. The treatment does carry the risk of triggering an allergic reaction. If approved, it will likely be covered under the pharmacy benefit.

Viaskin Peanut, by DBV Technologies, for children with peanut allergy aged 4 to 11 years is the second drug in development to protect against accidental exposure to peanuts. Viaskin delivers small quantities of the allergen via a skin or dermal patch containing 250 micrograms of peanut protein (about a quarter of a peanut), applied daily. According to the manufacturer, the treatment avoids the risk of exposure via the bloodstream and therefore much of the potential for adverse side effects. Although most patients are expected to develop sustained protection, they may need to receive treatment for life. If approved, Viaskin Peanut will likely be covered under the pharmacy benefit. FDA approval is expected in August 2020.

Palforzia is expected to cost between $3,000 and $20,000 a year, according to the company, while analysts estimate Viaskin Peanut to cost about $6,500.
CVS Health constantly monitors the pipeline and proactively develops and implements strategic cost management tools. Prior to launch, we seek input from external thought leaders so that we can model potential impact. We also have dedicated resources including experienced clinicians who closely follow and evaluate the drug pipeline to determine appropriate formulary placement and potential designation as a specialty drug. At launch, new-to-market review and an assessment of clinical appropriateness inform strategic plan design options, such as utilization management, including use of prior authorization, formulary management, such as tiered placement, and step therapy requirements.

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*Unless otherwise specified, these values represent total potential U.S. candidates based on anticipated indication and disease prevalence calculations; they do not reflect drug market share vs. competitors.

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