

Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever-changing environment

April 2020

NEW DRUG INFORMATION

- **Zeposia™ (ozanimod):** The U.S. Food and Drug Administration (FDA) granted approval to Bristol Myers Squibb's Zeposia an oral treatment for relapsing multiple sclerosis (RMS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. The FDA's approval was based on two Phase 3 clinical trials, SUNBEAM and RADIANCE, which compared Zeposia to Biogen's Avonex® (interferon beta-1a). In both clinical trials, Zeposia met its primary endpoint of relative reduction in annualized relapse rate (ARR) compared to Avonex. Additionally, at years one and two, Zeposia treatment reduced a greater number of brain lesions compared with Avonex.¹ Zeposia will directly compete with Novartis' Gilenya® (fingolimod), and Novartis' Mayzent® (siponimod). Bristol Myers Squibb touts that Zeposia is the only S1P receptor modulator that does not require patients to get a genetic test before starting treatment and does not require monitoring patients after their first dose.² Zeposia is currently in development for ulcerative colitis and Crohn's disease. The most common adverse reactions in patients being treated with Zeposia was upper respiratory infection. Due to the COVID-19 pandemic, Bristol Myers Squibb has made the decision to monitor the environment and will partner with the neurology community to inform launch timing and pricing to follow.
- **Sevenfact™ [coagulation factor VIIa (recombinant)-jncw]:** The FDA has granted approval to Laboratoire Francais du Fractionnement et des Biotechnologies' Sevenfact for treatment and control of bleeding episodes occurring in adults and adolescents 12 years of age and older with hemophilia A or B with inhibitors (neutralizing antibodies). Sevenfact is from genetically engineered rabbits, with the active ingredient as recombinant analog of human Factor VIIa (rhFVIIa). Sevenfact's approval was based on data from a clinical study that evaluated 27 patients with hemophilia A or B with inhibitors which included treatment of 465 mild or moderate, and three severe bleeding episodes. At 12 hours after treatment 86% of patients with mild or moderate bleeds were successfully treated with 75mcg/kg followed by subsequent doses of 225mcg/kg dose. The study included three severe bleeding episodes that were treated successfully with the higher dose of Sevenfact.³ Sevenfact will be available as a lyophilized powder in single-use vials containing 1mg or 5mg or coagulation factor VIIa (recombinant)-jncw. Sevenfact's launch and pricing are pending.

- **Koselugo™ (selumetinib):** Merck and AstraZeneca's Koselugo has been approved by the FDA for the treatment of pediatric patients, two years of age and older, with neurofibromatosis type 1 (NF1) who have symptomatic inoperable plexiform neurofibromas (PN). NF1 is a rare genetic condition that affects one in every 3,000 to 4,000 individuals. PNs, or tumors growing inside the patient's nerve sheaths, occur in 30 to 50% of patients with NF1. Koselugo is the first FDA approved treatment for these patients. The approval of Koselugo was based on Phase 2 trial, SPRINT Stratum 1, that demonstrated an overall response rate (ORR) of 66% (patients who have had at least a 20% reduction in tumor volume).⁴ All patients had a partial response and 82% of responders had a sustained response lasting at least 12 months. Koselugo's wholesale acquisition cost (WAC) is approximately \$12,500 per month. It will launch as soon as possible.⁵
- **Jelmyto™ (mitomycin gel):** The FDA has approved UroGenPharma's Jelmyto for treatment of low-grade upper tract urothelial cancer (LG UTUC). Jelmyto chemotherapy is formulated as a gel for instillation using UroGen's RTGel sustained-release, hydrogel-based platform. It is an alkylating drug that inhibits the transcription of DNA into RNA, stopping protein synthesis and prohibiting the cancer cell from multiplying. Jelmyto is administered via catheter by a health care provider once a week for six weeks. Jelmyto was approved based on the Phase 3 OLYMPUS trial, that demonstrated complete response at three months after initiation in 71 patients with low-grade upper tract urothelial cancer who had not been previously treated. Fifty-eight percent of patients achieved complete response after six weeks; 46% of patients continued to demonstrate complete response at 12 months.⁶ Jelmyto is set to launch by the second quarter of 2020 with pricing to follow.
- **Tukysa™ (tucatinib):** Seattle Genetics' Tukysa has been approved in combination with Teva's Herzuma® (trastuzumab-pkrb) and Genentech's Xeloda® (capecitabine) for the treatment of adult patients with advanced forms of HER2-positive breast cancer that can't be removed with surgery, or has spread to other parts of the body, including the brain, and who have received one or more prior treatments. The FDA approval is based on HER2CLIMB, a Phase 2 clinical trial comparing Tukysa in combination against trastuzumab and capecitabine alone. Tukysa demonstrated that in combination with trastuzumab and capecitabine patients had a 46% reduction in the risk of cancer progression or death (progression-free survival (PFS)). The addition of Tukysa reduced the risk of death by 34% compared to trastuzumab and capecitabine alone. HER2CLIMB showed that Tukysa reduced the risk of cancer PFS by 52% in patients that had brain metastases.⁷ Seattle Genetics plans to launch by the end of April with a WAC of \$18,500 for a 30-day supply.⁸
- **Pemazyre™ (pemigatinib):** The FDA approved Incyte's Pemazyre, a kinase inhibitor indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test. Pemazyre was approved based on FIGHT-202, a Phase 2 study that demonstrated an overall response rate (ORR) of 35% and a median duration of response of 9.1 months.⁹ Pemazyre is also being evaluated in bladder cancer, solid tumors and 8p11 myeloproliferative syndrome, with clinical trials on track for 2021. Incyte plans on launching Pemazyre as soon as possible, with a list price of \$17,000 per treatment cycle. A single patient would have an average treatment duration of six months and eight or nine cycles, which would have an average WAC of \$136,000–\$150,000.¹⁰
- **Trodely™ (sacituzumab govitecan-hziy):** The FDA approved Immunomedics' Trodely as an antibody drug conjugate (ADC) for treatment of patients with metastatic triple-negative breast cancer (mTNBC) who previously received at least two prior therapies for metastatic disease. These are typically more aggressive tumors that do not carry receptors for estrogen, progesterone, or human epidermal growth factor. Trodely was approved based on Phase 2 study that demonstrated an overall response rate (ORR) of 33.3% and a median duration of response of 7.7 months. Continued approval may be contingent upon verification of clinical benefit in confirmatory Phase 3, ASCENT study, which was recently halted by the independent Data Safety Monitoring Committee (DSMC) for compelling evidence of efficacy across multiple endpoints.¹¹ ASCENT is projected to complete study by mid-2020. In January 2019, Immunomedics received a complete response letter (CRL) from the FDA who asked for more information on the manufacturing element, citing problems with data integrity at the company's New Jersey plant where the medication was being produced. In November 2019, Immunomedics resubmitted. Immunomedics is ready to launch Trodely as soon as possible with pricing to follow.

NEW INDICATIONS

- **Epclusa® (sofosbuvir and velpatasvir):** The FDA broadened the use of Gilead Sciences' Epclusa to treat hepatitis C virus (HCV) in children ages six years and older or weighing at least 37 pounds (17 kilograms) with any of the six HCV genotypes — or strains — without cirrhosis (liver disease) or with mild cirrhosis. Previously, Epclusa was only approved for adult patients.
- **Opdivo® (nivolumab) plus Yervoy® (ipilimumab):** The FDA expanded the indication for Bristol-Myers Squibb's Opdivo to include treatment in patients with advanced hepatocellular carcinoma (HCC) that were previously treated with the kinase inhibitor sorafenib (Bayer's Nexavar®).
- **Eucria® (crisaborole):** The FDA expanded its indication for Pfizer's Eucria for topical treatment of mild to moderate atopic dermatitis in children aged three months up to two years. Eucria was previously only approved for patients ages two years and older.
- **Braftovi® (encorafenib):** The FDA approved a new indication for the BRAF kinase inhibitor for use in combination with cetuximab (Erbix®) in a doublet regimen for treatment of advanced BRAF V600E-mutant metastatic colorectal cancer (mCRC) patients following one or two lines of therapy.

APRIL NEWS

- "Gilead Sciences has made major mid-study changes to its global remdesivir trials, quadrupling the enrollment target and switching the primary endpoint. The changes come as the world waits for results from the Chinese clinical trials of the advanced COVID-19 antiviral candidate. Remdesivir's position at the front of the pack of potential COVID-19 drugs and vaccines has made it a very closely watched therapeutic. In that heightened environment, any information about the drug and its development is being scrutinized for hints about whether the therapy is likely to work, making Gilead's updates to its ClinicalTrials.gov listings notable events."¹¹
- "Including vaccines and treatments, the number of COVID-19-related clinical trials tripled during March—from 53 as of March 1 to 152 as of March 29, according to research by Geoffrey C. Porges, MBBS, senior research analyst at SVB Leerink. The largest number of these clinical phase therapeutics (49) were antivirals, followed by 46 small molecule drugs, 26 biologics, 18 plasma/cell derived treatments, and only 4 vaccines. Among the 18 candidates in our leading "Front Runner" category are several drugs that have garnered considerable media attention, including Gilead's Remdesivir, Inovio's INO-4800, Regeneron/Sanofi's Kevzara® (sarilumab), Roche/Genentech's Actemra (tocilizumab), and Distributed Bio's bioengineered antibodies."¹²
- "When it comes to AstraZeneca blockbuster Tagrisso, Wolfe Research analyst Tim Anderson laid things out simply in a Friday note to clients: "A major new commercial opportunity just opened up." At the recommendation of an Independent Data Monitoring Committee, the drugmaker will unblind a phase 3 trial of Tagrisso in postsurgery patients with EGFR-mutated non-small cell lung cancer two years ahead of schedule after the drug posted a significant benefit. By Anderson's calculations, sales of Tagrisso — which generated \$3.2 billion last year on the back of 71% year-over-year growth — could leap to \$4.5 billion in 2020 and \$8 billion by 2030."¹³
- "Just weeks following the FDA's emergency approval of hydroxychloroquine after President Trump repeatedly advocated its use for Covid-19, new data from a quick VA study highlighted an added risk of death with the drug. Drawing on the retrospective analysis of outcomes of 368 male VA patients, investigators concluded that patients taking hydroxychloroquine — a malaria drug — had a 27.8% death rate, well over twice the 11.4% death rate in the group who were not treated with hydroxychloroquine. The arm using hydroxychloroquine alone had a slightly higher rate of death than the 22.1% who were treated with hydroxychloroquine plus azithromycin, but that relatively small difference could have been triggered by other factors."¹⁴

YELLOW STICKER

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