

# Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever changing environment

July 2020

## NEW DRUG INFORMATION

- **Tazverik™ (tazemetostat):** The U.S. Food and Drug Administration (FDA) granted accelerated approval for Epizyme’s Tazverik in adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies. Tazverik applied for approval through a distinct new drug application (NDA) for this new indication of an already approved medication. Epizyme plans on consolidating this approval with its original NDA that was approved for epithelioid sarcoma in January 2020. The FDA’s approval is based on a Phase 2 trial that demonstrated Tazverik had an overall response rate (ORR) of 69% with 12% of patients achieving a complete response and 57% achieving a partial response. The median duration of response was 10.9 months.<sup>1</sup> The FDA’s approval requires Epizyme to conduct a confirmatory study, expand enrollment in Phase 2 cohort and conduct several post-marketing evaluations. Tazverik’s annual wholesale acquisition cost (WAC) is estimated at \$186,000.
- **Fintepla™ (fenfluramine):** Zogenix’s Fintepla has been approved by the FDA for treatment of seizures associated with Dravet syndrome. Dravet syndrome affects one out of every 15,700 babies born in the United States. Fintepla provides a low dose of fenfluramine that was in the “phen-fen” obesity combination that was withdrawn from the market in the 1990s due to concerns about cardiac safety. Fintepla’s approval was based on data from two Phase 3 clinical trials that cut convulsive seizures by 62% vs placebo.<sup>2</sup> Clinical trials demonstrated a reduction of convulsive seizures within three to four weeks, with the effects remaining consistent for 14 to 15 weeks. Fintepla will be launched by the end of July through a restricted distribution program, called the Fintepla Risk Evaluation and Mitigation Strategy (REMS) program. The REMS require echocardiograms to be performed before treatment, every six months during treatment and once three to six months after treatment ends. Its label will include a box warning about the association with vascular heart disease and pulmonary arterial hypertension. Fintepla uses weight-based dosing and will have an average annual WAC of \$96,000 per year.<sup>3</sup>

- **Mycapssa™ (octreotide):** The FDA has approved Chiasma's Mycapssa for maintenance treatment of adults with acromegaly. Mycapssa is an oral version of somatostatin analogs, a group of injectable drugs that slow the overproduction of growth hormones that lead to serious complications in patients with acromegaly. Mycapssa's approval is based on Phase 3 CHIASMA OPTIMAL trial, which measured the insulin-like growth factor 1 (IGF-1) level in patients compared to placebo.<sup>4</sup> Patients on therapy being able to maintain mean IGF-1 levels within the normal range at the end of treatment. Chiasma plans to launch Mycapssa in the fourth quarter 2020, with a remote launch through telehealth. Mycapssa will have an estimated list price of \$61,824 for the 40mg starting dose.<sup>5</sup>
- **Phesgo™ (pertuzumab, trastuzumab and hyaluronidase-zzxf):** Genentech's Phesgo has been approved four months early by the FDA as a fixed-dose combination of Roche's Perjeta® (pertuzumab), a HER2 dimerization inhibitor and Roche's Herceptin® (trastuzumab), an anti-HER2 antibody formulated with Halozyme's recombinant human hyaluronidase PH20-based Enhance technology for treatment of HER2-positive breast cancer. Phesgo combines two monoclonal antibodies in a single subcutaneous (SC) injection that can be administered at home by a health care professional. It takes eight minutes for the initial dose of Phesgo and about five minutes for each maintenance dose compared to 2.5 hours for the intravenous (IV) loading dose of the individual agents and 60-150 minutes for maintenance infusions of individual agents. Approval of Phesgo is based on a clinical trial that evaluated Phesgo SC compared to IV pertuzumab and trastuzumab concurrently. Phesgo demonstrated noninferiority in efficacy and safety.<sup>6</sup> Additionally, data from the Phase 2 PHRANCESCA study showed that 85% of patients preferred Phesgo SC due to less time in the clinic and more comfortable administration compared with IV formulations of pertuzumab and trastuzumab. Phesgo initial loading dose costs \$12,707 and the monthly cost as a maintenance treatment is \$12,300 which estimates WAC from \$55,000-\$151,000.<sup>7</sup>
- **Dojolvi™ (triheptanoin):** Ultragenyx's Dojolvi has been approved by the FDA as a medium-chain triglyceride indicated as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD). LC-FAOD are a group of rare, life-threatening genetic disorders in which the body is not able to convert long-chain fatty acids into energy. Dojolvi was approved based on Phase 2 study that compared the efficacy of Dojolvi to trioctanoin (8-carbon chain fatty acid) which demonstrated both treatment arms had similar mean changes from baseline in left ventricular ejection fraction and wall mass on resting echocardiogram. Additionally, an open-label Phase 2 study showed patients treated with Dojolvi led to a 48% reduction in the mean annualized rate of major clinical events (aggregate of events related to hypoglycemia, cardiomyopathy and rhabdomyolysis).<sup>8</sup> Ultragenyx has launched Dojolvi with a price of \$4,875 per vial or an estimated annual WAC of \$138,000 per patient.<sup>9</sup>
- **Hulio™ (adalimumab-fkjp):** The FDA has approved Mylan's Hulio, a biosimilar of AbbVie's Humira® (adalimumab) for the treatment of patients with rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adults Crohn's disease, ulcerative colitis and plaque psoriasis. Humira is additionally approved for the treatment of certain patients with pediatric Crohn's disease, hidradenitis suppurativa, and uveitis.<sup>10</sup> Hulio is the sixth biosimilar of Humira to obtain FDA approval. Hulio, along with other biosimilars of Humira, are planned to launch in 2023 with pricing to follow.

- **Inqovi™ (cedazuridine and decitabine):** Astex Pharmaceuticals' Inqovi has been approved by the FDA for treatment of adults with previously untreated intermediate- and high-risk myelodysplastic syndrome (MDS), including chronic myelomonocytic leukemia (CMML). Inqovi is a cytidine deaminase inhibitor that permits oral delivery of the hypomethylating agent decitabine as a fixed-dose combination tablet. The FDA recommended dose of Inqovi is one tablet (35mg decitabine and 100mg cedazuridine) taken orally on an empty stomach once daily on days one through five of each 28-day cycle. Inqovi allows patients to administer medication as an outpatient treatment. Inqovi was approved based on data from Phase 3 study, ASCERTAIN, which evaluated the five-day decitabine exposure equivalence of oral Inqovi and IV decitabine. Inqovi met its primary endpoint of total five-day decitabine area-under-the-curve (AUC) equivalence of oral C-DEC and IV decitabine.<sup>11</sup> Similar products include Janssen's Dacogen® (decitabine IV), Celgene's Vidaza® (azacitidine IV), and Celgene's Revlimid® (lenalidomide). Astex Pharmaceuticals launch and price of Inqovi are pending.
- **Xywav™ (calcium, magnesium, potassium, and sodium oxybates):** The FDA approved Jazz Pharmaceuticals' Xywav for treatment of cataplexy and excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. Xywav is a next-generation oxybate formulation with 92% less sodium than Xyrem® (sodium oxybate) and with other cations including calcium, magnesium and potassium. Jazz Pharmaceuticals notes that Xywav's decrease sodium intake may decrease risk of heart disease in comparison to the company's sister drug Xyrem. The Drug Enforcement Administration (DEA) has scheduled Xywav as a controlled substance schedule III. The FDA has approved Xywav based on a Phase 3 clinical trial in which patients taking Xywav experienced lower rates of cataplexy attacks and excessive daytime drowsiness compared to placebo.<sup>12</sup> Jazz Pharmaceuticals will launch by the end of 2020 following Risk Evaluation and Mitigation Strategy (REMS) implementation with pricing to follow.

## NEW INDICATIONS

- **Recarbrio® (imipenem, cilastatin and relebactam):** The FDA granted approval of Merck's Recarbrio for treatment of adults with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). Recarbrio was initially approved in July 2019 for complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI).
- **Keytruda® (pembrolizumab):** The FDA approved Merck's Keytruda to include three new indications and one new dosing schedule option. Keytruda is now approved for the treatment of patients with recurrent and/or metastatic cSCC that is not curable by surgery or radiation, for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer, and as monotherapy in adult and pediatric patients with unresectable or metastatic solid tumors with tissue tumor mutational burden-high (TMB-H)  $\geq 10$  mutations/megabase, as determined by an FDA-approved test, who have progressed following prior treatment and who have no satisfactory alternative treatment options. Keytruda's new dosing schedule option for the PD-1 inhibitor immuno-oncologic for a 400mg dose every six weeks infusion over 30 minutes for Keytruda indications in melanoma, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, gastric cancer, hepatocellular carcinoma and Merkel cell carcinoma.
- **Cosentyx® (secukinumab):** The FDA granted approval of Novartis' Cosentyx for treatment of non-radiographic axial spondyloarthritis (nr-axSpA).

- **Ilaris® (canakinumab):** The FDA expanded the indication of Novartis' Ilaris to include treatment of active Still's disease, including AOSD and SJIA in patients aged two years and older.
- **Crysvita® (burosumab-twza):** The FDA expanded Kyowa Kirin's Crysvita indication to include the treatment of FGF23-related hypophosphatemia associated with phosphaturic mesenchymal tumors (tumor-induced osteomalacia, or TIO) that cannot be curatively resected or localized.
- **Cyramza® (ramucirumab):** The FDA approved Lilly's Cyramza for use in combination with erlotinib for first-line treatment of metastatic non-small cell lung cancer (NSCLC) with EGFR exon 19 deletions or exon 21 (L858R) mutations.
- **Reblozyl® (luspatercept-aamt):** The FDA expanded Acceleron's Reblozyl indication to include treatment of adults with very low to intermediate risk myelodysplastic syndromes (MDS)-associated anemia who have ring sideroblasts and require red blood cell (RBC) transfusions.
- **Darzalex® (daratumumab):** The FDA has approved Janssen's new formulation of Darzalex as a subcutaneous formulation for multiple myeloma. The new formulation allows for five-minute administration.
- **Sirturo® (bedaquiline):** The FDA expanded Johnson & Johnson's Sirturo indication to include a new pediatric 20mg tablet for the diarylquinoline antimycobacterial agent for treatment of pulmonary multidrug resistant (MDR) tuberculosis (TB) in patients aged five years or more up to age 12 who weigh at least 15 kg.
- **Xpovio® (selinexor):** Karyopharm's Xpovio has been approved by the FDA to include treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least two prior multi-agent therapies and who are ineligible for stem cell transplantation, including CAR-T (chimeric antigen receptor modified T-cell) therapy. Additionally, Xpovio has a new indication as a single agent to treat relapsed or refractory diffuse large B-cell lymphoma (DLBCL).
- **Dupixent® (dupilumab):** The FDA approved a new 300mg auto-injector formulation of Sanofi's Dupixent as a single press injection with visual and audio feedback.
- **Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab):** The FDA granted Genentech's Tecentriq expanded indication to include treatment of people with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

## JULY NEWS

- “Bluebird bio, Inc. announced that new data from its ongoing Phase 1/2 HGB-206 study of investigational LentiGlobin™ gene therapy for adult and adolescent patients with sickle cell disease (SCD) show a near-complete reduction of serious vaso-occlusive crises (VOCs) and acute chest syndrome (ACS).”<sup>13</sup>
- “Aducanumab’s fate will be a test of how far the FDA and its commissioner, Stephen Hahn, M.D., are willing to diverge from its established approval standards. Under U.S. law, companies need to show “substantial” evidence of effectiveness to win approval. Biogen will arrive at the FDA with results from one trial that suggest aducanumab is no better than placebo and data from another that link it to improved scores on a dementia scale. The data underpinning the filing come from two phase 3 studies dubbed EMERGE and ENGAGE that tested aducanumab in patients with early-stage and mild Alzheimer’s, as well as from a phase 1b study. There was a discrepancy between the phase 3 studies — patients in the EMERGE trial who got the highest dose of aducanumab had a statistically significant improvement on a clinical dementia scale, but the same patient group in the ENGAGE study did worse than patients taking placebo on that same measure, as well as on a test of cognitive function. What’s more, the phase 3 program flunked a futility analysis in March 2019, leading Biogen to pull the plug on the studies, but the company about-faced eight months later, saying the analysis was “incorrect.” Biogen argued the futility analysis was based on a smaller data set that featured fewer patients who received high-dose aducanumab. Adding in the additional data showed aducanumab reduced clinical decline, the company said.”<sup>14</sup>
- “Intercept Pharmaceuticals, Inc., a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, announced that the FDA has issued a Complete Response Letter (CRL) regarding the New Drug Application (NDA) for obeticholic acid (OCA) for the treatment of fibrosis due to nonalcoholic steatohepatitis (NASH). The CRL indicated that, based on the data the FDA has reviewed to date, the Agency has determined that the predicted benefit of OCA based on a surrogate histopathologic endpoint remains uncertain and does not sufficiently outweigh the potential risks to support accelerated approval for the treatment of patients with liver fibrosis due to NASH. The FDA recommends that Intercept submit additional post-interim analysis efficacy and safety data from the ongoing REGENERATE study in support of potential accelerated approval and that the long-term outcomes phase of the study should continue.”<sup>15</sup>

## REFERENCES

1. <https://www.businesswire.com/news/home/20200618005820/en/%C2%A0Epizyme-Announces-U.S.-FDA-Accelerated-Approval-TAZVERIK%E2%84%A2>
2. [https://www.prnewswire.com/news-releases/fda-approves-fintepla-fenfluramine-for-the-treatment-of-seizures-associated-with-dravet-syndrome-301084208.html#:~:text=Zogenix%2C%20Inc.&text=\(NASDAQ%3A%20ZGNX\)%2C%20a,years%20of%20age%20and%20older.](https://www.prnewswire.com/news-releases/fda-approves-fintepla-fenfluramine-for-the-treatment-of-seizures-associated-with-dravet-syndrome-301084208.html#:~:text=Zogenix%2C%20Inc.&text=(NASDAQ%3A%20ZGNX)%2C%20a,years%20of%20age%20and%20older.)
3. <https://www.biopharmadive.com/news/zogenix-fintepla-fda-approval-dravet-syndrome/580608/>
4. <https://www.globenewswire.com/news-release/2020/06/26/2054210/0/en/Chiasma-Announces-FDA-Approval-of-MYCAPSSA-Octreotide-Capsules-the-First-and-Only-Oral-Somatostatin-Analog.html#:~:text=On%20June%2026%2C%202020%2C%20Chiasma,analog%20approved%20by%20the%20FDA.>
5. <https://www.fiercepharma.com/marketing/chiasma-secures-long-awaited-fda-nod-for-acromegaly-tablet-mycapssa-years-after-near#:~:text=Mycapssa%20will%20launch%20at%20a,a%20Friday%20call%20with%20analysts.>
6. <https://voice.ons.org/news-and-views/fda-approves-combination-of-pertuzumab-trastuzumab-and-hyaluronidase-zzxf-for-her2?ref=HP#:~:text=On%20June%2029%2C%202020%2C%20the,have%20not%20received%20prior%20anti>
7. <https://www.bizjournals.com/sanfrancisco/news/2020/06/29/cancer-genentech-fda-phesgo-herceptin-perjeta.html>
8. <https://www.empr.com/home/news/dojovi-approved-for-molecularly-confirmed-long-chain-fatty-acid-oxidation-disorders/>
9. <https://www.biopharmadive.com/news/ultragenyx-fda-approval-dojovi/580892/#:~:text=Like%20other%20rare%20disease%20medications,price%20of%20%244%2C875%20per%20vial.>
10. <https://www.bigmoleculerwatch.com/2020/07/07/fda-approves-mylans-biosimilar-of-humira-adalimumab/>
11. <https://astx.com/astx-pharmaceuticals-announces-u-s-food-and-drug-administration-fda-acceptance-for-review-of-an-nda-for-the-combination-oral-hypomethylating-agent-cedazuridine-and-decitabine-astx727-oral-c-de/>
12. <https://www.fiercepharma.com/marketing/jazz-s-xywav-a-low-sodium-alternative-to-blockbuster-xyrem-snags-fda-nod-narcolepsy>
13. <http://investor.bluebirdbio.com/news-releases/news-release-details/new-data-show-near-elimination-sickle-cell-disease-related-vaso>
14. <https://www.fiercebiotech.com/biotech/a-test-for-hahn-s-fda-biogen-submits-controversial-alzheimer-s-drug-aducanumab>
15. <https://www.globenewswire.com/news-release/2020/06/29/2054576/0/en/Intercept-Receives-Complete-Response-Letter-from-FDA-for-Obeticholic-Acid-for-the-Treatment-of-Fibrosis-Due-to-NASH.html>