PRIME THERAPEUTICS®

Specialty Pipeline **MONTHLY UPDATE**

Critical updates in an ever changing environment

May 2020

NEW DRUG INFORMATION

- **Bafiertam™ (monomethyl fumarate delayed-release):** The U.S. Food and Drug Administration (FDA) granted approval of Banner Life Sciences' Bafiertam for treatment of adults with relapsing forms of multiple sclerosis. In November 2018, the FDA granted tentative approval of Bafiertam through the 505(b)(2) pathway using Biogen's Tecfidera® (dimethyl fumarate) as a reference drug. Bafiertam met the required bioequivalence, safety, efficacy and quality standards compared with Tecfidera but final approval was based on expiration of Biogen's patent which was set to expire in June 2020. In April 2020, Banner Life Sciences announced that the United States Court of Appeals for the Federal Circuit had decided Bafiertam did not infringe on Tecfidera's patent.[1] Tecfidera generated $3.758 billion in U.S. annual sales in 2019. Bafiertam launch and pricing are pending.

- **Tabrecta™ (capmatinib):** Novartis' Tabrecta was granted accelerated approval by the FDA as a mesenchymal-epithelial transition (MET) inhibitor for treatment of first-line and previously treated patients with locally advanced or metastatic MET exon 14 skipping (METex14) mutated non-small cell lung cancer (NSCLC). The FDA also approved FoundationOne™ CDx as the companion diagnostic for Tabrecta, which detects mutations that lead to MET exon 14 skipping in tumor tissue. Tabrecta's approval was based on GEOMETRY, a Phase 2 clinical trial that demonstrated a confirmed overall response rate (ORR) of 68% and 41% among treatment-naive and previously treated patients respectively which was defined by tumor shrinkage in patients. Tabrecta also demonstrated that patients had a median duration response of 12.6 months in treatment-naive patients and 9.7 months in previously treated patients.[2] Novartis is currently conducting confirmatory trials of Tabrecta. Novartis has moved completely to digital promotion of Tabrecta. Novartis has launched Tabrecta with a wholesale annual cost (WAC) of $17,950 for a 28-day supply.[3]

- **Retevmo™ (selpercatinib):** Lilly's Retevmo was granted accelerated approval from the FDA for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC), and the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy, or advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). The FDA approved Retevmo based on Phase 1/2 trial, LIBETTO-001, which tested three subsets of patients.

Retevmo demonstrated an objective response rate (ORR) of 79% in RET fusion-positive thyroid cancer patients who had been previously treated and 100% for new RET fusion-positive thyroid cancer patients. Retevmo shrank tumors by 64% in patients with RET fusion-positive NSCLC who had been previously treated and 84% in patients who hadn't received previous treatment.[4] Lilly is currently conducting two clinical benefit confirmatory trials for Retevmo. Retevmo should only be used in patients whose tumors have a RET fusion in NSCLC or thyroid cancer or a RET mutation in MTC; however, at this time there is not an FDA-approved test for the detection of RET fusion and RET mutations. Patients can be determined through biomarker testing. Retevmo has launched and is available through specialty pharmacies with a WAC of $20,600 for a 30-day supply.[5]

- **Fensolvi™ (leuprolide acetate):** The FDA approved Tolmar Pharmaceuticals' Fensolvi for the treatment of pediatric patients two years of age and older with central precocious puberty (CPP). Fensolvi is an injected gel that releases leuprolide acetate in a sustained and controlled manner over time. Fensolvi is a 0.375ml, subcutaneous injection that is administered twice a year in a health care office. The FDA approved Fensolvi based on Phase 3 study that demonstrated 87% of children achieved a serum luteinizing hormone concentration of <4 IU/L at six months post injection. The study also demonstrated that Fensolvi suppressed sex hormones to pre-pubertal levels and stopped or reversed the progression of clinical signs of puberty.[4] Other similar products include AbbVie's Lupron Depot-Ped® (leuprolide acetate kit), Tolmar Pharmaceuticals' Eligard® (leuprolide acetate kit) and their generics. Tolmar Pharmaceuticals launched Fensolvi with a wholesale annual cost (WAC) of $27,093 per box.
- **Qinlock™ (ripretinib):** The FDA approved Deciphera pharmaceuticals' Qinlock for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with three or more kinase inhibitors, including imatinib. Qinlock's approval was based on Phase 3 INVICTUS study which demonstrated a median progression-free survival of 6.3 months compared to 1.0 month in the placebo arm. Qinlock additionally reduced the risk of disease progression or death by 85% compared to placebo. Deciphera Pharmaceuticals plans to launch Qinlock by the end of May with pricing to follow.

NEW INDICATIONS

- **Imbruvica® in combination with rituximab:** The FDA broadened the use of AbbVie and Janssen's Imbruvica for first-line treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- **Imfinzi® (durvalumab):** The FDA expanded the indication for AstraZeneca's Imfinzi in combination with etoposide and either carboplatin or cisplatin for first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).
- **Nerlynx® (neratinib):** The FDA approved a new indication for Puma's Nerlynx in combination with Roche's Xeloda® (capecitabine) for the third-line or greater treatment of patients with HER2-positive metastatic breast cancer who have failed two or more prior lines of HER2-directed therapy.
- **Rubraca® (rucaparib):** The FDA approved a new indication for Clovis Oncology's Rubraca, a poly (ADP-ribose) polymerase (PARP) inhibitor, to be used as monotherapy for treatment of adults with BRCA1/2-mutant recurrent, metastatic castrate-resistant prostate cancer (CRPC).

- **Opdivo® (nivolumab) plus Yervoy® (ipilimumab):** The FDA expanded the indication for Bristol-Myers Squibb's Opdivo as a first line treatment for patients with metastatic non-small cell lung cancer whose tumors express PD-L1 (≥1%), as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
- **Lynparza® (olaparib):** The FDA added a new indication for AstraZeneca's PARP inhibitor, Lynparza, for use in combination with Genentech's Avastin® (bevacizumab) for maintenance treatment of ovarian cancer patients who are in complete or partial response to first-line platinum-based chemotherapy with bevacizumab.

MAY NEWS

- "SMA is rare, affecting per 8,000 to 10,000 people globally, but represents a lucrative battle-ground for these drugmakers. Spinraza, launched in late 2016, carries a list price of $750,000 for the first year and $375,000 annually thereafter. Zolgensma — only approved for patients under the age of two — caused sticker shock with its $2.1 million price tag and the inevitable pushback from payers. This, despite Zolgensma's manufacturer, Novartis has emphasized that its five-year installment plan and curative potential makes it worth it. With Roche's plan to make risdiplam cheaper than Spinraza, the appeal of oral administration could make the drug an even bigger threat to the Spinraza franchise — which generated nearly $2.1 billion last year — compared to the world's most expensive therapy, Zolgensma. The FDA said it needed another three months to review additional data on the drug submitted by its makers."[8]
- "Genfit's bid to make R&D history with a storybook turnaround came to a crashing halt as the French biotech acknowledged that its Phase 3 study of elafibranor failed to distinguish itself from placebo in treating NASH. The biotech had tried to prove that the drug would resolve NASH without fibrosis in a population of more than 1,000 patients. But the data came up with a 19.2% response rate for the drug arm compared to a 14.7% rate for the placebo."[9]
- "In recent days and weeks, companies in the COVID-19 vaccine race have continuously updated the public about their manufacturing plans and inked collaborations to help with mass production—even ahead of seeing clinical data. Pfizer has tagged three U.S. sites—plus one in Belgium—for its rollout. The company aims to deliver millions of doses by the end of 2020 and hundreds of millions next year. Through its two manufacturing partnerships—with Emergent BioSolutions and with Catalent—J&J is setting up for a big push; Stoffels recently told ABC the company plans to supply 1 billion doses next year. And part of the reason vaccine giants Sanofi and GSK decided to partner in COVID-19 was to combine their global scale, execs said. The companies believe they can deliver hundreds of millions of doses annually starting in 2021. Novavax, which has been involved in other emerging disease vaccine research but hasn't brought any products to market, says it's aiming to produce 100 million doses by the end of the year and more than 1 billion in 2021. The company recently scored up to $384 million from the Coalition for Epidemic Preparedness Innovations, the group's largest grant to date."[10]

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