

Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever changing environment

August 2020

NEW DRUG INFORMATION

- **Tecartus™ (brexucabtagene autoleucel):** The U.S. Food and Drug Administration (FDA) granted accelerated approval for Kite's Tecartus for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL). Tecartus is the third CD19-targeting chimeric antigen receptor (CAR) T-cell therapy approved. Tecartus has the same construct as Kite's Yescarta® (axicabtagene ciloleucel). However, a primary point of differentiation comes from the T-cell enrichment that is part of Kite's XLP manufacturing process for Tecartus. The approval of this one-time therapy is based on results of ZUMA-2, a single-arm, open-label study which demonstrated 87% of patients responded to a single infusion of Tecartus, including 62% of patients achieving a complete response.¹ Kite will be creating a risk evaluation and mitigation strategy (REMS) infrastructure for Tecartus, combined with Yescarta. Tecartus has launched with a wholesale acquisition cost (WAC) \$373,000 per one-time treatment.
- **Monjuvi™ (tafasitamab-cxix):** The FDA approved MorphoSys' Monjuvi in combination with lenalidomide to treat adults with relapsed/refractory diffuse large B cell lymphoma (r/r DLBCL). Monjuvi targets the CD-19, a protein on the surface of B-cells that is also targeted by two already approved CAR-T therapies: Novartis' Kymriah® (tisagenlecleucel) and Gilead's Yescarta® (axicabtagene ciloleucel). Monjuvi is, however, an antibody that can be scaled, stored and taken off-the-shelf when a patient needs it. Thus, it is easier to make and deliver, compared to traditional CAR-T therapy. Monjuvi is the first approved treatment for adult DLBCL patients who progressed on or after first-line therapy. Monjuvi's approval was based on the Phase 2 L-MIND trial, which demonstrated a 55% overall response rate (ORR), a 37% complete response rate and a partial response rate of 18%. The median duration of response was 21.7 months, which was a key secondary endpoint for the trial.² Monjuvi has launched and uses weight-dosing with a WAC of \$1,200 per 200mg vial.
- **Blenrep™ (belantamab mafodotin):** GlaxoSmithKline's Blenrep has been approved by the FDA as a monotherapy treatment for relapsed or refractory multiple myeloma in patients whose prior therapy included an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. Approval of Blenrep is based on the Phase II DREAMM-2 trial, where patients had received an average of seven prior lines of therapy. Blenrep demonstrated a 31% ORR at six months.³ Blenrep had a 77% rate of ocular adverse events which led to a boxed warning and will only be available through a risk evaluation and mitigation strategy. The REMS requirements include prescriber and facility certification, patient counseling and enrollment in a monitoring program. Blenrep has launched with a WAC of \$8,277 per 100mg vial.

- **Evrysdi™ (risdiplam):** The FDA approved Genentech's Evrysdi for the treatment of spinal muscular atrophy (SMA) in patients two months of age and older. Evrysdi is the third FDA-approved treatment for SMA and the first oral, at-home treatment. Biogen, Inc.'s Spinraza® (nusinersen) is delivered intrathecally with a list price of \$750,000 for the first year of treatment and \$375,000 for each subsequent year. Novartis' Zolgensma® (onasemnogene abeparvovec-xioi) is a one-time gene therapy with a list price of \$2.1 million. Approval of Evrysdi was based on four Phase 2 or Phase 3 trials, FIREFISH, SUNFISH, JEWELFISH, and RAINBOWFISH, which evaluated safety and efficacy in a wide range of SMA patients.
 - The FIREFISH trial evaluated dose-escalation in infants with SMA type 1 and assessed safety. FIREFISH demonstrated that 29% of infants with SMA type 1, ages 1 to 7 months treated with Evrysdi were able to sit without support at 12 months of treatment for five seconds, which met its primary goal.⁴ Almost all untreated infants with infantile-onset SMA cannot sit independently.
 - SUNFISH is the first placebo-controlled trial to include adults with Types 2 and 3 SMA measuring Motor Function Measure-32 scale (MFM32) as its primary endpoint. Preliminary results demonstrate clinically meaningful improvements in MFM32 scale, 78.1% when treated with Evrysdi compared to 52.9% with placebo.⁴ This trial will conclude in September 2023. Evrysdi will launch by the end of August with a Genentech spokesperson stating the cost maxes out at \$340,000 annually and could be under \$100,000 for an infant weighing 15 pounds who is less than two years old.⁵
- **Viltepso™ (viltolarsen):** Nippon Shinyaku's Viltepso injection has been approved by the FDA for the treatment of patients with Duchenne muscular dystrophy (DMD) who are amenable to exon 53 skipping therapy. DMD with exon 53 skipping accounts for about 8% of DMD patients. Dystrophin is a key protein for supporting muscle health, and a lack of dystrophin is an underlying cause of DMD. Viltepso's clinical trial measured the increase in dystrophin as a primary endpoint for the treatment of DMD. Approval of Viltepso was based on a clinical trial that demonstrated 100% of patients (8/8) showed an increase in dystrophin level after treatment with 80mg/kg/week. Additionally, 88% of patients (7/8) showed dystrophin levels of 3% or greater than normal. Overall, after 20 – 24 weeks of treatment, a mean increase in dystrophin expression, to nearly 6% of normal was observed with Viltepso versus 0.6% at baseline.⁶ Viltepso's FDA accelerated approval requires Nippon Shinyaku to complete the confirmatory Phase III RACER53 trial, assessing time to stand for DMD patients with this confirmed mutation. Sarepta Therapeutics' Vyondys 53® (golodirsen) was the first FDA approved exon 53 skipping medication. Viltepso launch and price are pending.
- **Enspryng™ (satralizumab-mwge):** The FDA approved Roche's Enspryng for the treatment for neuromyelitis optica spectrum disorder (NMOSD). Enspryng is a self-administered, subcutaneous injection given once every four weeks. Enspryng is a monoclonal antibody that targets interleukin-6 (IL-6) receptor activity, which is believed to play a key role in the inflammation associated with NMOSD. Enspryng's approval was based on two Phase 3 clinical trials, SAKURASTAR and SAKURASKY, which both had a primary endpoint of time to first protocol-defined relapse. SAKURASTAR demonstrated 76.5% of Enspryng patients were relapse-free at 96 weeks, compared to 41.1% with placebo. SAKURASKY had 91.1% of Enspryng-treated patients were relapse-free at 96 weeks, compared to 56.8% with placebo.⁷ Enspryng will be available in the United States by the end of August. The annual WAC for Enspryng is just under \$220,000 for the first year when 15 doses are needed, and \$190,000 for subsequent years when 13 doses are required.⁸

NEW INDICATIONS

- **Cosentyx® (secukinumab):** The FDA granted approval of Novartis' Cosentyx for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA).
- **Ilaris® (canakinumab):** The FDA approved Novartis' Ilaris for the treatment of active Still's disease, including AOSD and SJIA in patients aged two years and older.
- **Crysvita® (burosumab-twza):** The FDA has approved a new indication for the monoclonal antibody, Crysvita, against the phosphaturic hormone FGF23 for 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):** Celgene's Reblozyl has been approved by the FDA for 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.
- **Brilinta® (ticagrelor) :** The FDA approved AstraZeneca's Brilinta to include a new indication to reduce the risk of a first MI or stroke in patients with coronary artery disease (CAD) at high risk for such events.
- **Darzalex® (daratumumab):** Janssen's Darzalex new subcutaneous formulation for multiple myeloma which would allow for five-minute administration has been approved by the FDA.
- **Sirturo® (bedaquiline):** Johnson & Johnson's Sirturo has been approved by the FDA to include the pediatric claim and new pediatric 20mg dose strength tablet for the diarylquinoline antimycobacterial agent for treatment of pulmonary multidrug resistant (MDR) tuberculosis (TB) in patients ages five to 12 who weigh at least 15 kg.
- **Xpovio® (selinexor):** The FDA has expanded Karyopharm's Xpovio's indication 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 therapy. This new indication is for Xpovio to be used as a single agent to treat relapsed or refractory DLBCL.
- **Dupixent® (dupilumab):** The FDA has approved a new formulation of Sanofi and Regeneron's Dupixent in a new 300mg auto-injector formulation. Prior to this approval, Dupixent was approved in pre-filled syringe, for treatment of certain patients with atopic dermatitis, eosinophilic asthma, and chronic rhinosinusitis with nasal polyposis.
- **Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab):** The FDA has approved Genentech's Tecentriq in combination with Avastin for the treatment of people with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.
- **Qwo® (Collagenase clostridium histolyticum (CCH)):** Endo International's Qwo has a new indication approved by the FDA for the combination of bacterial collagenases (approved as Xiaflex® for Depuytren's contracture and Peyronie's disease) for injectable treatment of cellulite in the buttocks.

- **Zejula® (niraparib):** GlaxoSmithKline's Zejula has a new indication approved by the FDA as a monotherapy maintenance treatment as first-line for women with advanced ovarian cancer who responded to platinum chemotherapy regardless of biomarker status.
- **Tremfya® (guselkumab):** The FDA approved Johnson & Johnson's Tremfya against the p19 subunit of interleukin-23 (IL-23) generated using MorphoSys' HuCAL technology for treatment of adults with active psoriatic arthritis (PsA).
- **Epidiolex® (cannabidiol):** The FDA approved an additional indication for GW Pharmaceuticals' Epidiolex to include the treatment of seizures associated with tuberous sclerosis complex (TSC) in patients one year of age and older.
- **Spravato® (esketamine):** Johnson & Johnson's Spravato has been approved to take in conjunction with an oral antidepressant to treat depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior.

SEPTEMBER NEWS

- "BioMarin Pharmaceutical Inc. today announced that the FDA issued a Complete Response Letter (CRL) to the Company's Biologics License Application (BLA) for valoctocogene roxaparvec gene therapy for severe hemophilia A on August 18, 2020. The FDA issues a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. Having previously agreed with the Agency on the extent of data necessary to support the BLA, the FDA introduced a new recommendation for two years of data from the Company's ongoing 270-301 study (Phase 3) to provide substantial evidence of a durable effect using Annualized Bleeding Rate (ABR) as the primary endpoint. The Agency first informed the Company of this recommendation in the CRL having not raised this at any time during development or review. The Agency recommended that the Company complete the Phase 3 Study and submit two-year follow-up safety and efficacy data on all study participants. FDA concluded that the differences between Study 270-201 (Phase 1/2) and the Phase 3 study limited its ability to rely on the Phase 1/2 study to support durability of effect. The Phase 3 study was fully enrolled in November 2019, and the last patient will complete two years of follow up in November 2021."⁹
- "The 28 players now in or close to the clinical race to get a Covid-19 vaccine over the finish line are angling for a piece of a multibillion-dollar market. And being first — or among the leaders will play a big role in determining just how big a piece. This is a snapshot of all the companies, universities and hospital-based groups now racing through the clinic, ranking them according to their place in the pipeline as well as the latest remarks available on timelines. And we'll keep this lineup updated right through the end of the year, as the checkered flags start to fall, possibly as early as October."¹⁰
- "The FDA has rejected Gilead's filing for approval of filgotinib in rheumatoid arthritis. With the FDA asking to see data from an ongoing clinical trial, Gilead is unlikely to be able to refile until toward the middle of next year, pushing it still further behind its rivals for the JAK inhibitor market. In disclosing the complete response letter, Gilead said the FDA has requested data from two ongoing clinical trials, MANTA and MANTA-RAY, that are assessing the effect of the 200mg dose of JAK1 inhibitor filgotinib on sperm concentrations. The FDA has also "expressed concerns regarding the overall benefit/risk profile of the filgotinib 200mg dose," according to Gilead."¹¹

- “Last year Sarepta hit center stage with the FDA’s controversial reversal of its CRL for the company’s second Duchenne muscular dystrophy drug — after the biotech was ambushed by agency insiders ready to reject a second pitch based on the same disease biomarker used for the first approval for eteplirsen, without actual data on the efficacy of the drug. The FDA approved the third Duchenne MD drug, based on the same biomarker. And regulators were ready to act yet again despite the lack of efficacy data.”¹²

REFERENCES

1. <https://www.gilead.com/news-and-press/press-room/press-releases/2020/7/us-fda-approves-kites-tecartus-the-first-and-only-car-t-treatment-for-relapsed-or-refractory-mantle-cell-lymphoma>
2. <https://www.biospace.com/article/fda-approves-morphosys-and-incyte-dlbc1-drug-monjuvi/>
3. <https://www.businesswire.com/news/home/20200806005336/en/Seattle-Genetics-Achieves-Milestone-Payment-Antibody-Drug-Conjugate>
4. <https://smanewstoday.com/2020/08/07/fda-approves-evrysdi-risdiplam-first-oral-sma-treatment/>
5. <https://endpts.com/fda-hands-out-a-quick-ok-for-potential-sma-blockbuster-risdiplam-handing-genentech-and-roche-a-chance-to-challenge-rivals-on-the-price/>
6. <https://www.prnewswire.com/news-releases/ns-pharmas-viltepso-viltolarsen-injection-now-fda-approved-in-the-us-for-the-treatment-of-duchenne-muscular-dystrophy-in-patients-amenable-to-exon-53-skipping-therapy-301111298.html>
7. <https://www.roche.com/media/releases/med-cor-2020-08-17.htm>
8. <https://www.reuters.com/article/us-roche-enspryng/roche-gets-u-s-approval-for-enspryng-takes-on-alexions-soliris-idUSKCN25B0J9#:~:text=The%20wholesale%20acquisition%20cost%20for,doses%20are%20required%2C%20Roche%20said>
9. <https://investors.biomarin.com/2020-08-19-BioMarin-Receives-Complete-Response-Letter-CRL-from-FDA-for-Valoctocogene-Roxaparvovec-Gene-Therapy-for-Severe-Hemophilia-A>
10. <https://endpts.com/28-players-are-in-or-about-to-jump-in-to-the-race-to-a-global-multibillion-dollar-market-for-a-covid-19-vaccine-heres-how-they-rank-so-far/>
11. <https://www.fiercebitech.com/biotech/fda-rejects-gilead-s-would-be-blockbuster-filgotinib-over-toxicity-concerns>
12. <https://endpts.com/fda-approves-duchenne-drug-viltepso-setting-up-showdown-with-sarepta-after-public-tit-for-tat/>