

Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever-changing environment

February 2021

NEW DRUG INFORMATION

- **Lupkynis™ (voclosporin):** The United States Food and Drug Administration (FDA) has approved Aurinia Pharma's Lupkynis in combination with a background immunosuppressive therapy regimen to treat adult patients with active lupus nephritis (LN). Lupkynis is the first oral treatment FDA approved for LN. Lupkynis was approved based on the Phase 3 clinical trial AURORA that demonstrated that Lupkynis, plus standard of care (SoC), was more than two times as effective at achieving a complete renal response than SoC alone.¹ Patients in the study taking Lupkynis also achieved a 50% reduction in urine protein creatinine ratio twice as fast as SoC, and a higher portion of Lupkynis-treated patients achieved a complete renal response at 24 weeks compared to patients receiving SoC. Lupkynis is administered as six capsules total a day in combination with SoC treatment (three 7.9mg capsule twice a day). Lupkynis has launched with limited distribution with a wholesale acquisition cost (WAC) of \$66 per 7.9mg capsule, or \$11,880 for 30 days at 23.7mg twice a day. According to Aurinia, Lupkynis has an average \$98,000 annual WAC which is for three of the 7.9mg capsules twice daily.
- **Ukoniq™ (umbralisib):** The FDA has approved TG Therapeutics' Ukoniq for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20 based regimen and adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy. Ukoniq is the first oral, once daily, inhibitor of phosphoinositide 3 kinase (PI3K) delta and casein kinase 1 (CK1) epsilon. Accelerated approval was granted for these indications based on 49% overall response rate (ORR) data with a 16% complete response (CR) from the Phase 2 UNITY-NHL trial.² Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial. TG Therapeutics has launched Ukoniq with a WAC of \$15,900 for 30-day supply.

- **Breyanzi™ (lisocabtagene maraleucel; liso-cel):** Bristol-Myers Squibb's Breyanzi has been approved as a CD19-directed chimeric antigen receptor (CAR) T-cell therapy for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B. Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma. A single dose of Breyanzi contains 50 to 110 x 10⁶ CAR-positive. Approval of Breyanzi was based on Phase 1 TRANSCEND NHL 001 that demonstrated an ORR of 73% and a CR 53%. Breyanzi did not reach the duration of response at six months (60.4%) and 12 months (54.7%).³ Breyanzi has launched as a one-time therapy with a \$410,300 annual WAC.⁴
- **Tepmetko™ (tepotinib):** The FDA approved EMD Serono's Tepmetko for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations. Tepmetko is a once daily dosing of two 225mg tablets (total 450mg). This indication is approved under accelerated approval based on a 43% ORR in both treatment-naïve patients and in previously treated patients. The median duration of response was 10.8 months for treatment-naïve patients and 11.1 months for previously treated patients.⁵ Duration of response of six months or more occurred among 67% of treatment-naïve patients and 75% of previously treated patients, and duration of response of nine months or more occurred among 30% of treatment-naïve patients and 50% of previously treated patients. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Tepmetko has launched with average wholesale price of \$25,078 per 30 days.
- **Evkeeza™ (evinacumab-dgnb):** Regeneron Pharmaceuticals' Evkeeza has been approved by the FDA as an adjunct to other low-density lipoprotein cholesterol (LDL-C) lowering therapies to treat adult and pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH). Evkeeza is the first FDA-approved treatment that binds to and blocks the function of angiotensin-like 3 (ANGPTL3), a protein that plays a key role in lipid metabolism. HoFH, also known as homozygous FH, is an ultra-rare inherited condition that affects approximately 1,300 patients in the U.S. Evkeeza was approved based on Phase 3 ELIPSE HoFH trial which met its primary endpoint by reducing LDL-C by 49% on average compared to placebo at week 24 (47% reduction in Evkeeza patients, 2% increase in placebo patients).⁶ Evkeeza will be exclusively distributed by Orsini Specialty Pharmacy and the average WAC per patient in the United States will vary based on weight, and is expected to be approximately \$450,000 per year on average.
- **Cosela™ (trilaciclib):** The FDA approved G1 Therapeutics' Cosela for injection to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC). It is the first therapy designed to help protect bone marrow when administered prior to chemotherapy treatment. Cosela is administered intravenously as a 30-minute infusion within four hours prior to the start of chemotherapy. Clinical trials demonstrated patients receiving Cosela prior to the start of chemotherapy had clinically meaningful and statistically significant reduction in the duration and severity of neutropenia.⁷ Cosela is expected to be commercially available through G1's specialty distributor partner network in early March with pricing to follow.

NEW INDICATIONS

- **Nplate® (romiplostim):** The FDA granted approval of Amgen's Nplate as a thrombopoietin receptor agonist indicated to increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome, or HSARS).
- **Opdivo® (nivolumab):** Bristol-Myers Squibb's Opdivo has been granted a new indication by the FDA to be used in combination with cabozantinib (Exelixis' Cabometyx®) for first-line treatment of advanced renal cell carcinoma (RCC).
- **Cabometyx® (cabozantinib):** The FDA approved Exelixis' Cabometyx new indication in combination with the immuno-oncologic nivolumab (Bristol-Myers Squibb's Opdivo®) for first-line treatment of advanced renal cell carcinoma (RCC).
- **Simponi Aria® (golimumab):** The FDA approved Johnson and Johnson's Simponi Aria expanded indication to include patients two years of age and older, for the treatment of active psoriatic arthritis (PsA) or active polyarticular juvenile idiopathic arthritis (pJIA).
- **Gavreto® (pralsetinib):** Blueprint Medicines' Gavreto additional indication has been approved by the FDA to include treatment of patients with advanced or metastatic RET mutant medullary thyroid cancer (MTC) and RET fusion-positive thyroid cancers.
- **Enhertu® (fam-trastuzumab deruxtecan-nxki):** The FDA expanded the indication of Daiichi Pharmaceutical's Enhertu to include treatment of patients with HER2-positive metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

FEBRUARY NEWS

- “The US Food and Drug Administration (FDA) has extended the review period for aducanumab, the investigational amyloid-clearing treatment for Alzheimer’s disease (AD), by 3 months, the drug’s manufacturers have announced. The updated prescription drug user fee act (PDUFA) action date has been pushed forward from March 7 to June 7. As part of the ongoing review, Biogen submitted a response to an information request by the FDA, including additional analyses and clinical data, which the FDA considered a major amendment to the application that will require additional time for review,” Biogen and Eisai said in a statement.”⁸
- “Bluebird bio has run into a fresh set of troubles for its gene therapy LentiGlobin. The biotech, which has seen its gene therapy work mired at the FDA due to CMC issues, revealed it had suspended work on its early-stage study as well as the Phase III sickle cell trial for LentiGlobin in order to investigate two more serious side effects among patients in the program. In addition, bluebird CEO Nick Leschly hit the brakes on marketing Zynteglo (betibeglogene autotemcel; beti-cel) in Europe, where it’s approved for beta thalassemia, because it uses the same BB305 lentiviral vector used in the gene therapy for sickle cell disease.”⁹
- “Amicus stock got hammered after the biotech put out word that the crown jewel in the pipeline just failed the primary endpoint in a head-to-head study with the standard of care for Pompe disease. The key setback came on the comparison between AT-GAA and Lumizyme in the 6-minute walk test, the gold standard for demonstrating efficacy. The numbers for a combined group of patients who were both switched from ERT therapy or ERT naive looked better, but not better enough to achieve statistical significance. This primary endpoint in the combined population was assessed for superiority and while numerically greater, statistical significance for superiority on this combined population was not achieved for the AT-GAA arm as compared to the alglucosidase alfa arm ($p=0.072$). Narrow that down to just the group that had switched from Lumizyme and there was still only a nominal improvement at a p value of 0.046. But where the drug failed, and failed badly, was in the group of patients who were treatment naive. On the 6 minute walk test, the Lumizyme arm did better than the Amicus drug. On the forced vital capacity, Lumizyme also outperformed, with an ugly p value for Amicus’ drug of 0.57.”¹⁰
- “A drug used to treat type 2 diabetes has been found to help obese and overweight people lose more weight than any other medicine on the market, according to a new study find. Semaglutide, the drug used in the trial, helps insulin get released from the pancreas in patients with type 2 diabetes, and it’s administered in doses of around 1mg. It’s sold under the brand name Ozempic, and has been found to suppress appetite, too. Over 68 weeks, participants who received the drug lost, on average, nearly 15% of their weight — a stark difference from members in the placebo group, who lost 2.4%. What’s more, the study also found that a third of participants who took semaglutide lost 20% of their weight.”¹¹

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