PRIME THERAPEUTICS®

Specialty Pipeline **MONTHLY UPDATE**

Critical updates in an ever changing environment

August 2021

NEW DRUG INFORMATION

- **Saphnelo™ (anifrolumab-fnia):** The U.S. Food and Drug Administration (FDA) approved AstraZeneca's Saphnelo (anifrolumab-fnia) as a treatment for adults with systemic lupus erythematosus (SLE) who are receiving standard therapy. Saphnelo is a first in class, fully human monoclonal antibody that binds to subunit 1 of the type I interferon (IFN) receptor, blocking the activity of type I IFNs. Type I IFNs play a role in the pathogenesis of SLE. Approximately 60–80% of adult patients with active SLE express elevated levels of type I IFN inducible genes. The approval of Saphnelo was based on efficacy and safety data from three clinical trials: TULIP 1 and 2, both Phase 3 clinical trials, and MUSE, a Phase 2 clinical trial. Efficacy of Saphnelo was established based on clinical response using the composite endpoints, the British Isles Lupus Assessment Group based Composite Lupus Assessment (BICLA) and the SLE Responder Index (SRI-4). In these trials, more patients treated with Saphnelo experienced a reduction in overall disease activity across organ systems, including skin and joints, and achieved sustained reduction in oral corticosteroid (OCS) use compared to placebo, with both groups receiving standard therapy. TULIP-1 did not meet its primary endpoint in the SRI-4 scale. SRI-4 response was 49% in the Saphnelo-treated patients versus 43% in placebo patients. TULIP-2 had a SRI-4 response of 62.8% in the Saphnelo-treated patients versus 38.8% in placebo patients which was not statistically significant. TULIP-2 did not meet its primary endpoint of BICLA. MUSE demonstrated a BICLA response of 47.8% in the Saphnelo treated patients versus 31.5% in the placebo patients.[1] Saphnelo will be available as a 300 mg/2mL solution in a single-dose vial. Saphnelo has launched with a wholesale acquisition price (WAC) of $4,600 per 28 days.
- **Uptravi® IV (selexipag):** Janssen Pharmaceutical Companies of Johnson & Johnson's Uptravi (selexipag) injection has been approved for intravenous (IV) use for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients with WHO functional class (FC) II–III, who are temporarily unable to take oral therapy. Uptravi IV is a therapeutic option that will allow patients to avoid short-term treatment interruptions and stay on Uptravi therapy, as uninterrupted treatment is considered key for individuals with PAH. The FDA approval was based on multi-center, open-label single sequence cross-over Phase 3 study that demonstrated the safety, tolerability and pharmacokinetics of temporarily switching between Uptravi tablets and Uptravi IV.[2] Uptravi IV launch and price are pending.

- **Nexviazyme® (avalglucosidase alfa-ngpt):** The FDA has approved Nexviazyme (avalglucosidase alfa-ngpt) for the treatment of patients one year of age and older with late-onset Pompe disease, a progressive and debilitating muscle disorder that impairs a person's ability to move and breathe. Nexviazyme is an enzyme replacement therapy (ERT) designed to specifically target the mannose-6-phosphate (M6P) receptor, the key pathway for cellular uptake of enzyme replacement therapy in Pompe disease. Nexviazyme's approval was based on the Phase 3 COMET trail that compared Nexviazyme's efficacy to its ERT predecessor alglucosidase alfa, which demonstrated Nexviazyme patients scored 2.4 points higher on a standard lung function test, compared to alglucosidase alfa.[3] This confirmed noninferiority but was not its statistical superiority over alglucosidase alfa. Additionally, patients treated with Nexviazyme were able to walk 30 meters farther in the six-minute walk test compared to patients treated with alglucosidase alfa. Nexviazyme is administered by a health care professional with weight-based dosing via intravenous infusion once every two weeks. Nexviazyme has launched with an average wholesale price (WAC) of $2057.88 per vial.[4]
- **Welireg® (belzutifan):** The FDA has approved Merck's Welireg for the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery. Welireg is an oral hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor. The approval of Walireg was based on results from the open-label Study 004 trial, where the major efficacy endpoint was overall response rate (ORR) in patients with VHL-associated RCC. Welireg demonstrated an ORR of 49%; all responses were partial responses. The median time to response was eight months. In patients with VHL-associated pancreatic neuroendocrine tumors, belzutifan showed an ORR of 83%, with a complete response rate of 17% and a partial response rate of 67%.[5] Welireg is scheduled to launch end of August or September with an annual WAC of $316,800.

NEW INDICATIONS

- **Nucala® (mepolizumab):** The FDA expanded the indication of Glaxo Smith Kline's Nucala for the treatment of chronic rhinosinusitis with nasal polyps.
- **Keytruda® (pembrolizumab):** Merck's Keytruda has been granted two additional indications by the FDA to include the treatment of patients with high-risk, early-stage triple negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment and then as a single agent as adjuvant treatment after surgery and for treatment of patients with high-risk, early-stage triple negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment and then as a single agent as adjuvant treatment after surgery.

AUGUST NEWS

- "Almost two years after the FDA ordered an abrupt halt to Novartis' testing of intrathecal delivery of Zolgensma, trials may finally resume. The Swiss drug maker says data from its non-human primate toxicology study have resolved all safety concerns regulators had, including any potential risks of dorsal root ganglia, about this route of administration. Novartis' next step will be initiating STEER, a pivotal Phase 3 study in SMA type 2 that will enroll 'treatment naïve patients who are between two and 18 years of age, able to sit, but have never walked.' Novartis had originally hoped to file a BLA for Zolgensma's intrathecal delivery as early as 2021. The FDA quashed those hopes when it placed the entire program on partial clinical hold, forcing the company to pause dosing of any new patients in the Phase I STRONG study and hold off treating patients in the REACH study, which reportedly involved other types of SMA."[6]

- "Now that the door at the FDA has been opened wide for Alzheimer's drugs that can demonstrate a reduction in amyloid, Biogen and its partners at Eisai are pushing for a quick OK on the next drug to follow in the controversial path of aducanumab. In a presentation to analysts, Eisai neurology chief Ivan Cheung outlined some bullish expectations for their newly approved treatment and set the stage for what he believes will be a fast follow for BAN2401 (lecanemab) — after a dry spell in new drug development that's lasted close to 20 years."[7]

- "The FDA is expected to approve Pfizer's coronavirus vaccine by early September, amid a resurgence of cases that has heightened pressure on the administration to get more Americans vaccinated. While the agency had long eyed the fall for granting full licensure, officials have recently accelerated their work, and now hope to finalize approval in a matter of weeks, according to three people familiar with the matter. Regulators authorized Pfizer's two-dose vaccine for emergency use last December, followed quickly by Moderna. But full approval is a higher bar that health officials hope will nudge hesitant Americans towards getting vaccinated."[8]

- "The folks at ICER have crunched the data on aducanumab. The independent drug watchdog brought together a panel of Alzheimer's experts to review the trial results, queried execs at Biogen and assessed the $56,000 price. And here's their final verdict that accompanies the detailed assessment: 'The clinical trial history and evidence regarding aducanumab are complex,' said David Rind, ICER's CMO. 'We have spent eight months analyzing the study results, talking with patient groups and clinical experts, and working with the manufacturer to understand their position. At the conclusion of this effort, despite the tremendous unmet need for new treatments for Alzheimer's disease, we have judged the current evidence to be insufficient to demonstrate that aducanumab slows cognitive decline, while it is clear that it can harm some patients.'"[9]

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