# PRESS RELEASE

**Banner Life Sciences Announces Final FDA Approval of BAFIERTAM for Multiple Sclerosis**

*BAFIERTAM™ (monomethyl fumarate), the bioequivalent alternative to Biogen's Tecfidera® (dimethyl fumarate), is a new oral treatment option for relapsing forms of multiple sclerosis*

*Open path to commercialization*

HIGH POINT, N.C., April 30, 2020 /Businesswire/ -- Banner Life Sciences LLC (Banner), a privately held specialty pharmaceutical company, announced today that the U.S. Food and Drug Administration (FDA) granted final approval of BAFIERTAM™ (monomethyl fumarate) delayed-release capsules for the treatment of relapsing forms of multiple sclerosis (MS).

"The FDA's final approval marks an important milestone for Banner and for patients living with relapsing-remitting multiple sclerosis," said Franck Rousseau, M.D., Chief Executive Officer of Banner. "We are working diligently and are eager to bring this alternative treatment to physicians and patients as soon as possible."

"As a practicing neurologist treating patients with MS, I'm encouraged that a lower dose of BAFIERTAM is equivalent to Tecfidera and may possibly lead to improved gastrointestinal tolerability for patients, especially early in the treatment regimen," said Daniel Wynn, M.D. FACNS FAASM, Director, Clinical Research, Director Consultants in Neurology Multiple Sclerosis Comprehensive Care Center, Chicago, Illinois.

The FDA granted tentative approval of BAFIERTAM on November 16, 2018 under a New Drug Application (NDA) submitted under the 505(b)(2) filing pathway. BAFIERTAM, a novel fumarate bioequivalent alternative to a prodrug of BAFIERTAM, Tecfidera®[1] (dimethyl fumarate) of Biogen Inc, met the required bioequivalence, safety, efficacy and quality standards for tentative approval. Final approval was pending the expiration of U.S. Patent Number 7,619,001 ("the '001 patent") on June 20, 2020 protecting Biogen's Tecfidera, or the outcome of pending litigation between Banner and Biogen regarding the patent.

In January 2019, Banner announced that the U.S. District Court for the District of Delaware had ruled in favor of Banner's motion for judgment on the pleadings against Biogen, Inc. deciding BAFIERTAM does not infringe the '001 patent, thus permitting Banner to seek final FDA approval. On April 21, 2020, Banner announced that the United States Court of Appeals for the Federal Circuit had upheld the earlier Court's decision.

**About BAFIERTAM™ (monomethyl fumarate)**

BAFIERTAM is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

**About Relapsing-Remitting Multiple Sclerosis**

Relapsing-remitting multiple sclerosis (RRMS), the most common form of MS, is a debilitating autoimmune disease characterized by inflammatory attacks to the central nervous system followed by periods of remission. RRMS affects approximately 85 percent of patients diagnosed with MS, or an estimated 2 million people worldwide.[2] There is no cure for MS and disease progression and degree of impairment vary widely by patient depending on the location and extent of nerve damage. Treatment regimens for RRMS focus on symptom management, slowing disease progression and reducing relapses.

**SELECTED SAFETY INFORMATION**

**CONTRAINDICATIONS**

BAFIERTAM is contraindicated in patients with known hypersensitivity to monomethyl fumarate, dimethyl fumarate, diroximel fumarate, or to any of the excipients of BAFIERTAM.

**WARNINGS AND PRECAUTIONS**

**Anaphylaxis and Angioedema -** BAFIERTAM can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms in patients taking dimethyl fumarate (the prodrug of BAFIERTAM) have included difficulty breathing, urticaria, and swelling of the throat and tongue. Patients should be instructed to discontinue BAFIERTAM and seek immediate medical care should they experience signs and symptoms of anaphylaxis or angioedema.

**Progressive Multifocal Leukoencephalopathy -** Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with dimethyl fumarate (the prodrug of BAFIERTAM). PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal case of PML occurred in a patient who received dimethyl fumarate for 4 years while enrolled in a clinical trial. During the clinical trial, the patient experienced prolonged lymphopenia (lymphocyte counts predominantly <0.5x109/L for 3.5 years) while taking dimethyl fumarate. The patient had no other identified systemic medical conditions resulting in compromised immune system function and had not previously been treated with natalizumab, which has a known association with PML. The patient was also not taking any immunosuppressive or immunomodulatory medications concomitantly.

PML has also occurred in patients taking dimethyl fumarate in the postmarketing setting in the presence of lymphopenia (<0.9x109/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts <0.8x109/L persisting for more than 6 months.

At the first sign or symptom suggestive of PML, withhold BAFIERTAM and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms. Cases of PML, diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. Many of these patients subsequently became symptomatic with PML. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Lower PML-related mortality and morbidity have been reported following discontinuation of another MS medication associated with PML in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.

**Herpes Zoster and Other Serious Opportunistic Infections -** Serious cases of herpes zoster have occurred with dimethyl fumarate (the prodrug of BAFIERTAM), including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis, and herpes zoster meningomyelitis. These events may occur at any time during treatment. Monitor patients on BAFIERTAM for signs and symptoms of herpes zoster. If herpes zoster occurs, appropriate treatment for herpes zoster should be administered.

Other serious opportunistic infections have occurred with dimethyl fumarate, including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. These infections have been reported in patients with reduced absolute lymphocyte counts (ALC) as well as in patients with normal ALC. These infections have affected the brain, meninges, spinal cord, gastrointestinal tract, lungs, skin, eye, and ear. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment.

Consider withholding BAFIERTAM treatment in patients with herpes zoster or other serious infections until the infection has resolved.

**Lymphopenia -** BAFIERTAM may decrease lymphocyte counts. In the MS placebo-controlled trials with dimethyl fumarate (the prodrug of BAFIERTAM), mean lymphocyte counts decreased by approximately 30% during the first year of treatment with dimethyl fumarate and then remained stable. Four weeks after stopping dimethyl fumarate, mean lymphocyte counts increased, but did not return to baseline. Six percent (6%) of dimethyl fumarate patients and <1% of placebo patients experienced lymphocyte counts <0.5x109/L (lower limit of normal 0.91x109/L). The incidence of infections (60% vs 58%) and serious infections (2% vs 2%) was similar in patients treated with dimethyl fumarate or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts

<0.8x109/L or <0.5x109/L in controlled trials, although one patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5x109/L for 3.5 years).

In controlled and uncontrolled clinical trials with dimethyl fumarate, 2% of patients experienced lymphocyte counts <0.5 x 109/L for at least six months, and in this group, the majority of lymphocyte counts remained <0.5x109/L with continued therapy. Neither BAFIERTAM nor dimethyl fumarate have been studied in patients with preexisting low lymphocyte counts.

Obtain a CBC, including lymphocyte count, before initiating treatment with BAFIERTAM, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated. Consider interruption of BAFIERTAM in patients with lymphocyte counts less than 0.5 x 109/L persisting for more than six months. Given the potential for delayed recovery of lymphocyte counts, continue to obtain lymphocyte counts until their recovery if BAFIERTAM is discontinued or interrupted because of lymphopenia. Consider withholding treatment from patients with serious infections until resolution. Decisions about whether or not to restart BAFIERTAM should be individualized based on clinical circumstances.

**Liver Injury -** Clinically significant cases of liver injury have been reported in patients treated with dimethyl fumarate (the prodrug of BAFIERTAM) in the postmarketing setting. The onset has ranged from a few days to several months after initiation of treatment with dimethyl fumarate. Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal and elevation of total bilirubin to greater than 2-fold the upper limit of normal have been observed. These abnormalities resolved upon treatment discontinuation. Some cases required hospitalization. None of the reported cases resulted in liver failure, liver transplant, or death. However, the combination of new serum aminotransferase elevations with increased levels of bilirubin caused by drug-induced hepatocellular injury is an important predictor of serious liver injury that may lead to acute liver failure, liver transplant, or death in some patients.

Elevations of hepatic transaminases (most no greater than 3 times the upper limit of normal) were observed during controlled trials with dimethyl fumarate.

Obtain serum aminotransferase, alkaline phosphatase (ALP), and total bilirubin levels prior to treatment with BAFIERTAM and during treatment, as clinically indicated. Discontinue BAFIERTAM if clinically significant liver injury induced by BAFIERTAM is suspected.

**Flushing -** BAFIERTAM may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). In clinical trials of dimethyl fumarate (the prodrug of BAFIERTAM), 40% of dimethyl fumarate-treated patients experienced flushing. Flushing symptoms generally began soon after initiating dimethyl fumarate and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued dimethyl fumarate for flushing, and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization. Studies with dimethyl fumarate show that administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to dosing may reduce the incidence or severity of flushing. In the BAFIERTAM studies, the presence of food did not impact the incidence of flushing.

**DRUG INTERACTIONS**

**Concomitant Dimethyl Fumarate or Diroximel Fumarate -** Both dimethyl fumarate and diroximel fumarate are metabolized to monomethyl fumarate. Therefore, BAFIERTAM is contraindicated in patients currently taking dimethyl fumarate or diroximel fumarate. BAFIERTAM may be initiated the day following discontinuation of either of these drugs.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy -** There are no adequate data on the developmental risk associated with the use of BAFIERTAM or dimethyl fumarate (the prodrug of BAFIERTAM) in pregnant women. Patients should call their healthcare provider if they are pregnant or plan to become pregnant because it is not known if BAFIERTAM will harm an unborn baby.

**Lactation -** There are no data on the presence of DMF or MMF in human milk. The effects on the breastfed infant and on milk production are unknown. Patients should call their healthcare provider if they are breastfeeding or plan to breastfeed because it is not known if BAFIERTAM passes into breast milk.

**Pediatric Use -** Safety and effectiveness in pediatric patients have not been established.

**Geriatric Use -** Clinical studies of dimethyl fumarate (the prodrug of BAFIERTAM) and of BAFIERTAM did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

**For more information, please see the full Prescribing Information for BAFIERTAM.**

**About Banner Life Sciences LLC**
Banner Life Sciences LLC, a privately held clinical-stage pharmaceutical company, combines a proven history of formulation expertise with proprietary technologies to create specialty pharmaceuticals that solve real unmet clinical needs.

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[1] Tecfidera® is a registered trademark of Biogen

[2] National Multiple Sclerosis Society

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