Biogen and Alkermes Announce FDA Approval of VUMERITY™ (diroximel fumarate) for Multiple Sclerosis

October 30, 2019

– VUMERITY, a New Oral Treatment Option for Relapsing Forms of MS, Offers a Combination of Well-Characterized Efficacy, Safety and Tolerability –

CAMBRIDGE, Mass. and DUBLIN, Ireland, Oct. 30, 2019 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) and Alkermes plc (Nasdaq: ALKS) today announced that the U.S. Food and Drug Administration (FDA) approved VUMERITY ™ (diroximel fumarate), a novel oral fumarate with a distinct chemical structure, for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease. Biogen holds the exclusive, worldwide license to commercialize VUMERITY and intends to make it available in the United States in the near future.

“The FDA’s approval of VUMERITY delivers on Biogen’s commitment to pursue new therapies that may provide meaningful impact for people living with relapsing MS, and we look forward to bringing it to the MS community as an additional treatment option,” said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president, research and development, and chief medical officer at Biogen. “VUMERITY is a novel fumarate that offers the well-characterized efficacy of TECFIDERA® (dimethyl fumarate) and has been studied for improved patient-reported gastrointestinal tolerability.”

“The approval of VUMERITY for relapsing MS marks the culmination of a multi-year development program and is the latest milestone in our mission to develop new treatments for patients living with chronic central nervous system disorders,” said Craig Hopkinson, M.D., chief medical officer and senior vice president of medicines development and medical affairs at Alkermes. “We are grateful to the patients and study investigators who have participated in our VUMERITY clinical trials and we look forward to working with our collaboration partners at Biogen to make this new treatment available to patients.”

The FDA approval of VUMERITY was based on a New Drug Application (NDA) submitted under the 505(b)(2) filing pathway. It included data from pharmacokinetic bridging studies comparing VUMERITY and TECFIDERA to establish bioequivalence, and relied, in part, on the FDA’s findings of safety and efficacy for TECFIDERA.

The NDA submission also included interim exposure and safety findings from EVOLVE-MS-1, an ongoing, Phase 3, single-arm, open-label, two-year safety study evaluating VUMERITY in patients with relapsing-remitting MS. Interim results from EVOLVE-MS-1 at the time of NDA submission included a low overall rate of VUMERITY treatment discontinuation due to adverse events (6.3 percent), and a rate of less than one percent of patients who discontinued VUMERITY treatment due to gastrointestinal (GI) adverse events. Additional exploratory efficacy endpoints in the ongoing EVOLVE-MS-1 study showed changes in clinical and radiological measures compared to baseline.

“MS is a heterogeneous disease, and real-world patient circumstances can vary, reinforcing the benefits of having therapeutic choices to support the diverse range of treatment considerations,” said Robert Naismith, M.D., professor of neurology, Washington University School of Medicine in St. Louis. “Throughout its clinical development program, VUMERITY has demonstrated a desirable therapeutic profile, making it a compelling new option for patients.”

“MS is a lifelong disease that has a significant impact on the people affected and their caregivers. We are encouraged by the progress being made in the treatment of MS, and pleased that another treatment option will soon be available,” said Bruce Bebo, Ph.D., executive vice president, research, National MS Society. “It’s important for people with MS to have treatments that are both efficacious and tolerable to help manage their disease.”

Under the terms of the license and collaboration agreement between Biogen and Alkermes, Biogen will pay Alkermes $150 million in connection with the FDA’s approval of VUMERITY. Biogen plans to account for this milestone payment as an asset that will be amortized over the expected useful life of the product. Alkermes is also entitled to receive a mid-teens percentage royalty on worldwide net commercial sales of VUMERITY, subject, under certain circumstances, to minimum annual payments for the first five years following FDA approval and customary reductions as set forth in the agreement.

Please see full **Prescribing Information** for VUMERITY.

About VUMERITY ™ (diroximel fumarate)
VUMERITY is a novel oral fumarate with a distinct chemical structure approved in the U.S. for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease. Once in the body, VUMERITY rapidly converts to monomethyl fumarate, the same active metabolite of dimethyl fumarate.

About the VUMERITY EVOLVE-MS Clinical Development Program
The key components of the EVOLVE-MS (**E**ndea**vo**ring to Advance Treatment for Patients **Liv**ing with Multipl**e** Sclerosis) clinical development program of VUMERITY include the EVOLVE-MS-1 study, a Phase 3, open-label, two-year safety study in relapsing-remitting multiple sclerosis (MS) patients, along with pharmacokinetic bridging studies comparing VUMERITY and TECFIDERA to demonstrate bioequivalence. The EVOLVE-MS clinical development program also includes the EVOLVE-MS-2 study, an elective Phase 3, five-week randomized, prospective, double-blind, multi-center study that assessed the gastrointestinal (GI) tolerability of VUMERITY and TECFIDERA using self-administered GI questionnaires.

INDICATION and IMPORTANT SAFETY INFORMATION for VUMERITY™ (diroximel fumarate)
What is VUMERITY™ (diroximel fumarate)?
VUMERITY is a prescription medicine used to treat people with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is not known if VUMERITY is safe and effective in children.

Important Safety Information
Who should not take VUMERITY?

Patients should not use VUMERITY if they have had an allergic reaction (such as welts, hives, swelling of the face, lips, mouth or tongue, or difficulty breathing) to diroximel fumarate, dimethyl fumarate, or any of the ingredients in VUMERITY or if they are taking dimethyl fumarate.

Before taking and while taking VUMERITY, patients should tell their healthcare provider if they: have liver problems; kidney problems; have or have had low white blood cell counts or an infection; are pregnant or plan to become pregnant because it is not known if VUMERITY will harm an unborn baby; are breastfeeding or plan to breastfeed because it is not known if VUMERITY passes into breast milk; are taking prescription or over-the-counter medicines, vitamins, or herbal supplements.

What should patients avoid while taking VUMERITY?
Patients should not drink alcohol at the same time they take a VUMERITY dose.

What are the possible side effects of VUMERITY?
VUMERITY may cause serious side effects including:

- **Allergic reaction** (such as welts, hives, swelling of the face, lips, mouth or tongue, or difficulty breathing).
- **PML (progressive multifocal leukoencephalopathy**), a rare brain infection that usually leads to death or severe disability over a period of weeks or months. Patients should tell their doctor right away if they get any of these symptoms of PML: weakness on one side of the body that gets worse, clumsiness in their arms or legs, vision problems, changes in thinking and memory, confusion, or personality changes.
- **Decreases in your white blood cell count,** the patient's healthcare provider should do a blood test to check their white blood cell count before starting treatment with VUMERITY and while on therapy. Patients should have bloods tests after 6 months of treatment and every 6 to 12 months after that.
- **Liver problems**, the patient's healthcare provider should do blood tests to check liver function before starting treatment with VUMERITY and during treatment if needed. Patients should tell their healthcare provider right away if they get any of these symptoms of a liver problem during treatment: severe tiredness, loss of appetite, pain on the right side of the stomach, have dark or brown (tea color) urine, or yellowing of the skin or the white part of the eyes.

The most common side effects of VUMERITY include: flushing, redness, itching, or rash; nausea, vomiting, diarrhea, stomach pain, or indigestion. Flushing and stomach problems are the most common reactions, especially at the start of therapy, and may decrease over time. Taking VUMERITY with food (avoid high-fat, high-calorie meal or snack) may help reduce flushing. Patients should call their healthcare provider if they have any of these symptoms, are bothered by them, or if they do not go away.

These are not all the possible side effects of VUMERITY. Patients should call their healthcare provider for medical advice about side effects. Patients may report side effects to FDA at 1-800-FDA-1088. **For more information go to dailymed.nlm.nih.gov.**

Please see the full Prescribing Information, including Patient Information for VUMERITY.

INDICATION and IMPORTANT SAFETY INFORMATION for TECFIDERA® (dimethyl fumarate)
What is TECFIDERA® (dimethyl fumarate)?
TECFIDERA 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. It is not known if TECFIDERA is safe and effective in children under 18 years of age.

Important Safety Information

Who should not take TECFIDERA?
Patients should not use TECFIDERA if they have had an allergic reaction (such as welts, hives, swelling of the face, lips, mouth or tongue, or difficulty breathing) to TECFIDERA or any of its ingredients.

Before taking and while taking TECFIDERA, patients should tell their healthcare provider if they have or have had: low white blood cell counts, an infection, or any other medical conditions.

Patients should tell their healthcare provider if they: are pregnant or plan to become pregnant, because it is not known if TECFIDERA will harm an unborn baby; patients should talk to their healthcare provider about enrolling in the TECFIDERA Pregnancy Registry if they become pregnant while taking TECFIDERA; the purpose of this registry is to monitor the health of the patient and baby and patients can enroll by calling 1-866-810-1462 or visiting www.tecfiderapregnancyregistry.com; are breastfeeding or plan to breastfeed because it is not known if TECFIDERA passes into breast milk; are taking prescription or over-the-counter medicines, vitamins, or herbal supplements.

What are the possible side effects of TECFIDERA?
TECFIDERA may cause serious side effects, including:

- **Allergic reaction** (such as welts, hives, swelling of the face, lips, mouth or tongue, or difficulty breathing).
- **PML,** a rare brain infection that usually leads to death or severe disability.
- **Decreases in your white blood cell count**, the patient's healthcare provider should do a blood test before starting treatment with TECFIDERA and while on therapy.
- **Liver problems,** the patient's healthcare provider should do blood tests to check liver function before starting treatment with TECFIDERA and during treatment if needed. Patients should tell their healthcare provider right away if they get any of these symptoms of a liver problem during treatment: severe tiredness, loss of appetite, pain on the right side of your stomach, have dark or brown (tea color) urine, yellowing of your skin or the white part of your eyes.

The most common side effects of TECFIDERA include: flushing, redness, itching, or rash; nausea, vomiting, diarrhea, stomach pain, or indigestion. Flushing and stomach problems are the most common reactions, especially at the start of therapy, and may decrease over time. Taking TECFIDERA with food may help reduce flushing. Patients should call their healthcare provider if they have any of these symptoms, are bothered by them, or if they do not go away. Ask your healthcare provider if taking aspirin before taking TECFIDERA may reduce flushing.

These are not all the possible side effects of TECFIDERA. Patients should call their healthcare provider for medical advice about side effects. Patients

may report side effects to FDA at 1-800-FDA-1088. **For more information go to dailymed.nlm.nih.gov.**

Please see full Prescribing Information, including Patient Information.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray, and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, commercializes biosimilars of advanced biologics, and is focused on advancing research programs in multiple sclerosis and neuroimmunology, neuromuscular disorders, movement disorders, Alzheimer's disease and dementia, ophthalmology, immunology, neurocognitive disorders, acute neurology and pain.

We routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

About Alkermes plc
Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines for the treatment of central nervous system (CNS) diseases and oncology. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for diseases that include schizophrenia, depression, addiction, multiple sclerosis and cancer. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

Biogen Safe Harbor
This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to the potential benefits, safety and efficacy of VUMERITY and TECFIDERA; potential clinical effects of VUMERITY and TECFIDERA; results from the EVOLVE-MS-1 and EVOLVE-MS-2 studies; the clinical development program for VUMERITY; the launch of VUMERITY, including the timing of the launch; Biogen's research and development program for the treatment of MS; the treatment of MS; the potential of Biogen's commercial business and pipeline programs, including VUMERITY and TECFIDERA; the anticipated benefits and potential of Biogen's collaboration arrangements with Alkermes; risks and uncertainties associated with drug development and commercialization; and Biogen's future financial and operating results. These forward-looking statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "except," "forecast," "goal," "intend," "may," "plan," "possible," "potential," "will," "would" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; risks of unexpected costs or delays; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of Biogen's drug candidates; unexpected concerns may arise from additional data, analysis or results obtained during clinical trials; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; uncertainty of success in the commercialization of VUMERITY; risks relating to the potential launch of VUMERITY, including preparedness of healthcare providers to treat patients, the ability to obtain and maintain adequate reimbursement for VUMERITY and other unexpected difficulties or hurdles; product liability claims; and third party collaboration risks. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this press release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

Alkermes Note Regarding Forward-Looking Statements
Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the potential therapeutic and commercial value of VUMERITY for the treatment of relapsing forms of MS; continued activities in the EVOLVE-MS clinical development program for VUMERITY; plans and expected timing for the commercial launch of VUMERITY by Biogen; and the financial and commercial benefits that may be achieved under the license and collaboration agreement between Alkermes and Biogen in connection with the approval and commercialization of VUMERITY. Alkermes cautions that forward-looking statements are inherently uncertain. Although Alkermes believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: whether clinical results for VUMERITY will be predictive of real-world results; whether VUMERITY, in real-world use, is shown to be unsafe or ineffective; whether VUMERITY receives reimbursement from government and third-party payers; whether there will be unexpected costs or delays in the commercial launch of VUMERITY; whether physicians and patients perceive VUMERITY as efficacious and well-tolerated; whether the potential financial and commercial benefits of collaboration with Biogen under the license and collaboration agreement between Alkermes and Biogen will be achieved; and those risks described in the Alkermes Annual Report on Form 10-K for the fiscal year ended Dec. 31, 2018 and in subsequent filings made by Alkermes with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

TECFIDERA® is a registered trademark of Biogen Inc.
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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/1af51ae4-577d-4558-ad41-7abe5a1dae24

A video accompanying this announcement is available at: https://www.globenewswire.com/NewsRoom/AttachmentNg/3191c160-3316-4e9c-bdd0-97ade134f441