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Adamas Announces Publication of ADS-5102 Phase 3 EASE LID Clinical Trial in JAMA Neurology

--Placebo-Controlled Phase 3 Trial Demonstrated that ADS-5102 Significantly Reduced Both Dyskinesia and OFF Time at Six Months in Parkinson's Disease Patients with Levodopa-induced Dyskinesia --

-- New Drug Application for ADS-5102 Currently Under FDA Review with August 24, 2017 PDUFA Date--

EMERYVILLE, Calif., June 12, 2017 (GLOBE NEWSWIRE) -- Adamas Pharmaceuticals, Inc. (Nasdaq:ADMS) today announced that results of its Phase 3 EASE LID clinical trial of ADS-5102 were published online in *JAMA Neurology.* A New Drug Application supporting ADS-5102 (amantadine) extended-release capsules for the treatment of levodopa-induced dyskinesia (LID) in people with Parkinson's disease is under review by the U.S. Food and Drug Administration with a Prescription Drug User Fee Act (PDUFA) action date of August 24, 2017. If approved, ADS-5102 will be the first and only medicine indicated for the treatment of LID in people with Parkinson's disease. The publication can be accessed at: http://jamanetwork.com/journals/jamaneurology/article-abstract/2630682.

"ADS-5102 reduced the duration, severity, and impact of dyskinesia in people with Parkinson's disease. These statistically significant reductions were maintained for the entirety of the six-month EASE LID study," stated Rajesh Pahwa, M.D., Laverne & Joyce Rider Professor of Neurology, Director of the Parkinson's Disease and Movement Disorder Center at the University of Kansas Medical Center. "Also meaningful is that ADS-5102 significantly reduced OFF time in the study. To my knowledge, ADS-5102 is the first and only drug with clinically demonstrated reductions in both dyskinesia and OFF time, conditions which impact physicians' ability to treat underlying Parkinson's disease in dyskinetic patients."

"ADS-5102, if approved, will be an important advancement in the treatment of Parkinson's disease. Many people with Parkinson's have levodopa-induced dyskinesias, and these can be troublesome and impact their quality of life," said Stanley Fahn, M.D., H. Houston Merritt Professor of Neurology and Director Emeritus of the Center for Parkinson's Disease and Other Movement Disorders at Columbia University in New York City. "This Phase 3 clinical trial shows that ADS-5102 can significantly reduce these dyskinesias, thus providing meaningful benefit."

The randomized, double-blind, placebo-controlled EASE LID study met its pre-specified primary endpoint demonstrating that patients who received ADS-5102 experienced a significantly greater decrease in LID at 12 weeks than those who received placebo (p=0.0009), as measured by the Unified Dyskinesia Rating Scale (UDysRS). This improvement was maintained at 24 weeks, with ADS-5102-treated patients again showing a significantly greater decrease than placebo-treated patients (p=0.0008). Additionally, the ADS-5102 group experienced significant improvements in key pre-specified, hierarchical secondary endpoints compared with the placebo group, as measured using the Parkinson's disease home diary. ADS-5102 treatment resulted in a statistically significant increase in ON time without troublesome dyskinesia and a statistically significant decrease in OFF time at 12 and 24 weeks. Adverse events (AEs) were reported for 89 percent of ADS-5102 patients and 60 percent of placebo patients, and most reported were mild to moderate. The most common AEs for ADS-5102 versus placebo were visual hallucinations, peripheral edema, and dizziness. No study drug-related serious AEs were reported. A total of 17 patients discontinued study treatment due to an AE (13 patients in the ADS-5102 group vs. four in the placebo group). The EASE LID trial results were previously presented at the 68th American Academy of Neurology Annual Meeting and at the 20th International Congress of Parkinson's Disease and Movement Disorders.

About ADS-5102 and its Clinical Development Program for Levodopa-induced Dyskinesia
ADS-5102 is a high-dose amantadine taken once daily at bedtime. ADS-5102 was designed to control the initial rate of rise in plasma concentration to mitigate the risk of central nervous system adverse events observed shortly after administration. This dosing regimen results in sustained high plasma levels of amantadine during morning and throughout waking hours when dyskinesia occurs, thereby improving the benefit-risk profile of the drug. If approved, ADS-5102 will meet a significant unmet need, as the first and only medicine approved for dyskinesia in people with Parkinson's disease.

The Phase 3 ADS-5102 levodopa-induced dyskinesia clinical program was conducted at movement disorder centers across the United States, Canada and Europe. The program included three placebo-controlled trials (Phase 2/3 EASED, Phase 3 EASE LID, and Phase 3 EASE LID 3), and an ongoing, long-term, open-label Phase 3 EASE LID 2 trial. The two placebo-controlled Phase 3 trials met their primary and all key secondary endpoints, and the pooled data at 12 weeks demonstrate:

- Primary endpoint: The UDysRS total score was -17.7 in the ADS-5102 group versus -7.6 in the placebo group ($p < 0.0001$); an improvement in the UDysRS total score of approximately 30 percent among those treated with ADS-5102 compared to placebo treated patients.
- Key secondary endpoints: ON time without troublesome dyskinesia improved by approximately 40 percent in the ADS-5102 group compared to placebo ($p < 0.0001$), which represents a 2.4 hour per day increase in ON time without troublesome dyskinesia, and decreased OFF time by approximately 45 percent compared to placebo ($p=0.0006$), which represents a one hour per day decrease in OFF time. In totality, patients treated with ADS-5102 in the Phase 3 studies gained approximately four hours of ON time without troublesome dyskinesia daily.
- Safety and tolerability data: In the Phase 3 EASE LID and EASE LID 3 trials, the most common adverse events were consistent with the known amantadine safety profile, and most occurred between Weeks 2-4 of treatment. The most common adverse reactions (≥5 percent in the active group) were visual hallucinations, dry mouth, dizziness, peripheral edema, falls, constipation, nausea, anxiety, decreased appetite, livedo reticularis, insomnia, auditory hallucinations and orthostatic hypotension. The majority (84 percent) of ADS-5102 treated patients did not discontinue study drug due to adverse reactions.

The Phase 3 EASE LID 2 long-term, open-label, safety and efficacy study of ADS-5102 is ongoing. Data were recently presented at the 21st International Congress of Parkinson's Disease and Movement Disorders. Results demonstrated that ADS-5102 was well tolerated and had a treatment effect on motor complications, as measured by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Part IV score, was demonstrated and maintained for up to 88 weeks.

Additionally, patients previously treated with amantadine immediate-release who switched to open-label ADS-5102 experienced a three point, statistically significant reduction in MDS-UPDRS Part IV at Week 8 and maintained out to Week 64. These results were comparable to previous placebo-treated patients, and patients who have undergone prior deep brain stimulation treatment.

The safety data are consistent with the previously reported safety profile of ADS-5102 and the known safety profile of amantadine.

About Parkinson's Disease and Levodopa-induced Dyskinesia
Parkinson's disease is a chronic neurodegenerative disorder affecting close to 1 million people in the United States. It is characterized by the progressive loss of dopaminergic neurons, causing lower levels of endogenous dopamine and manifesting as symptoms of bradykinesia (slowness of movement), rigidity, impaired walking, tremor and postural instability.

Levodopa, which replaces lost dopamine, is the most effective therapy for all stages of Parkinson's disease and is considered the "gold standard" therapy. Over time, people require increasingly higher or more frequent doses of levodopa in order to avoid the recurrent periods of OFF time when the underlying symptoms of Parkinson's disease return. As Parkinson's disease progresses, nearly all people on levodopa therapy will also experience LID, which is characterized by involuntary movements that are non-rhythmic, purposeless, and unpredictable. Symptoms of OFF time are characterized by slowness of movement, rigidity, impaired walking, tremor, and postural instability. These people often experience multiple fluctuating periods of OFF time and dyskinesia during any given day, which can impede their movement and daily function. In the United States, approximately 150,000 to 200,000 people with Parkinson's suffer from LID.

About Adamas Pharmaceuticals, Inc.
Adamas develops new medicines to improve the daily lives of those affected by chronic neurologic disorders, including Parkinson's disease, multiple sclerosis, epilepsy, and Alzheimer's disease. Adamas has pioneered a platform to develop medicines for chronic neurologic disorders based on an understanding of the time-dependent biologic processes responsible for disease activity and drug response. The company's most advanced product candidate, ADS-5102, is a high-dose amantadine, taken once daily at bedtime, in development for levodopa-induced dyskinesia in people with Parkinson's disease and for the treatment of walking impairment in people with multiple sclerosis. A New Drug Application supporting ADS-5102 for the treatment of levodopa-induced dyskinesia in people with Parkinson's disease is under review by the FDA with a PDUFA date of August 24, 2017. Adamas is exploring other indications for further development of ADS-5102. Adamas is also investigating ADS-4101 for the treatment of partial onset seizures in patients with epilepsy. Additionally, Adamas' licensed assets, are currently marketed by Allergan under the brand names NAMENDA XR® and NAMZARIC®, and Adamas is eligible to receive royalties on sales of these medicines beginning in June 2018 and May 2020, respectively. For more information, please visit www.adamaspharma.com.

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Forward-looking Statements
Statements contained in this press release regarding matters that may occur in the future are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including but not limited to, statements contained

in this press release regarding the potential approval of ADS-5102 for the treatment of levodopa-induced dyskinesia in people with Parkinson's disease and the potential clinical benefits of ADS-5102. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. For a description of risks and uncertainties that could cause actual results to differ from those expressed in forward-looking statements, including risks relating to Adamas' research, clinical, development and commercial activities relating to ADS-5102 and ADS-4101, the regulatory and competitive environment and Adamas' business in general, see Adamas' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 9, 2017. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release. Adamas undertakes no obligation to update any forward-looking statement in this press release.

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