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Algernon Pharmaceuticals Launches Stroke Treatment Clinical Research Program with Psychedelic Drug DMT “The Spirit Molecule”

VANCOUVER, British Columbia, Feb. 01, 2021 (GLOBE NEWSWIRE) -- Algernon Pharmaceuticals Inc. (CSE: AGN) (FRANKFURT: AGW) (OTCQB: AGNPF) (the “Company” or “Algernon”) a clinical stage pharmaceutical development company is pleased to announce that it has established a clinical research program for the treatment of stroke focused on AP-188 (“N,N-Dimethyltryptamine or DMT”), a known psychedelic compound that is part of the tryptamine family (other drugs in the tryptamine family include psilocybin and psilocin). Algernon plans to be the first company globally to pursue DMT for stroke in humans and is planning to begin a clinical trial as soon as possible in 2021.

Algernon has also filed new provisional patents for new forms of DMT, in addition to formulation, dosage and method of use claims for ischemic stroke. The Company has also filed claims for combination therapy of DMT and Constraint Induced Movement Therapy (“CIMT”).

The Company announced in early January that it would be establishing a new clinical research program in Q1 2021 to add to its current pipeline. Repurposing DMT from its psychedelic effects to a new potential treatment for stroke could have a positive impact on the millions of people that suffer the debilitating consequences of a stroke each year.

The Company’s decision to investigate DMT and move it into human trials for stroke is based on multiple independent, positive preclinical studies demonstrating that DMT helps promote neurogenesis as well as structural and functional neural plasticity. These are key factors involved in the brain’s ability to form and reorganize synaptic connections, which are needed for healing following a brain injury.

A recently published preclinical study in an animal model for stroke, showed that rats treated with DMT recovered motor function more quickly and to a greater extent, and also exhibited lower lesion volumes when compared to control group animals that did not receive DMT. Key data from the study achieved statistical significance.

Unlike other companies recently researching psychedelic drugs, Algernon will be focusing on a sub-hallucinogenic, or microdose of DMT provided by continuous intravenous administration. By pursuing a continuous active microdose, the goal will be to provide patients with the therapeutic benefits of DMT, without having a psychedelic experience. This is an important element when considering treating a patient who has just suffered a stroke, wherein medications that cause a hallucinogenic response would cause unwanted confusion and stress.

The Company also believes that a microdosing approach to developing a DMT treatment may enable a much wider review and acceptance of its data, including garnering the early interest of research investigators, the interest of clinical trial patients, and ultimately clinical acceptance. Algernon's approach may also allow for a quicker pathway to regulatory approval including a Breakthrough Therapy designation from the U.S. FDA, which enables priority review of a drug candidate if preliminary clinical trials indicate that the therapy may offer substantial treatment advantages over existing options for patients with serious or life-threatening diseases.

"While other research is exploring DMT for its hallucinogenic qualities and effects, Algernon will be working to unlock DMT's non-psychedelic potential to help promote healing and recovery in the brain from a stroke, one of the most devastating injuries a human being can experience," said Christopher J. Moreau, CEO of Algernon Pharmaceuticals. "The Algernon team, which now includes global experts in DMT and stroke research, is uniquely positioned to quickly repurpose DMT into human trials in the most cost and time effective way possible, just as we did with Ifenprodil in the on-going Phase 2 trial for Idiopathic Pulmonary Fibrosis ("IPF") and chronic cough, as well as with our on-going COVID-19 trial."

A Streetsmart *LIVE* webcast interview that explains the new clinical program in greater detail can be found here: Algernon Streetsmart *LIVE* Interview

Global Stroke Treatment Market: Overview

According to a 2019 report from Transparency Market Research:

- The global stroke treatment market was valued at ~US$ 8 Bn in 2018.
- Projected to grow at a compound annual growth rate of ~7% over the forecast period, the global stroke treatment market is expected to reach a value of ~US$ 15 Bn by the year 2027.
- Rise in the prevalence of stroke across the world, surge in the elderly patient pool, and rapid rise in comorbidities such as atrial fibrillation, diabetes, and hypertension leading to high risk of developing stroke are anticipated to drive the global stroke treatment market during the forecast period.
- North America is the leading regional market in the global stroke treatment market, and will continue to have a major share throughout the forecast period of 2019 to 2027.

DMT Background

N,N-Dimethyltryptamine, or DMT, is a hallucinogenic tryptamine drug producing effects similar to those of other psychedelics like LSD, ketamine, psilocybin and psilocin. DMT occurs naturally in many plant species and animals and has been used in religious ceremonies as a traditional spiritual medicine by indigenous people in the Amazonian basin. DMT can also be synthesised in a laboratory.

At higher doses, DMT has a rapid onset, intense psychedelic effects, and a relatively short duration of action with an estimated half-life of less than fifteen minutes. Like other hallucinogens in the tryptamine family, DMT binds to serotonin receptors to produce euphoria and psychedelic effects. Because the effects of DMT do not last very long, it has been referred to in some circles as the "businessman's trip".

Named the “Spirit Molecule” by Dr. Rick Strassman, an American clinical associate professor of psychiatry and DMT research pioneer, DMT has been shown to induce neuroplasticity in a number of key preclinical studies. DMT is believed to activate pathways involved with forming neuron connections and has been shown in studies to increase the number of dendritic spines on cortical neurons. Dendritic spines form synapses (connections) with other neurons and are a major site of molecular activity in the brain.

While Dr. Strassman’s Phase 1 bolus intravenous human study identified the sub-hallucinogenic dose of DMT in humans, another preclinical animal study demonstrated this same dose level still retains the neuroplastic effect seen in higher hallucinogenic doses.

Algernon will be investigating an intravenous sub-hallucinogenic dose of DMT in its research and clinical studies.

DMT – Building the Case for Stroke

Data from a study published in *Experimental Neurology*, in May 2020 showed that in a rat model of cerebral ischemia-reperfusion injury, DMT reduced the infarct (dead cells) volume and improved functional recovery.

Key Findings:

- Animals treated with DMT displayed lower lesion volumes than control animals measured by MRI 24 hours following the occlusion. ($p = 0.0373$)

- Animals in the DMT group improved motor function more quickly and to a greater extent than the control group; The differences became significant on the 4^{th} day ($p = 0.0325$) and persisted throughout a 30-day follow-up.

- mRNA expression of brain-derived neurotrophic factor (BDNF) was upregulated in both the peri-infarct cortex ($p = 0.0273$) and contralateral cortex ($p = 0.0048$) as well as in serum ($p < 0.0001$). BDNF is a key facilitator of neuroplasticity.

The full study can be viewed at the following link:

https://www.sciencedirect.com/science/article/abs/pii/S0014488620300765?via%3Dihub

Algernon’s Preclinical Research Plan

The Company will be conducting a number of preclinical research experiments to guide the Company as it advances towards it planned clinical trials. Studies will include:

1. Potency of multiple new forms of DMT
2. Toxicology
3. Treatment timing and duration
4. DMT in combination with CIMT

The Company has identified several of countries that allow research with tryptamines as well as Contract Research Organization’s (CRO’s) with experience in this area of research which have the required approvals to work with controlled substances.

Algernon's DMT Clinical Research Plan

1. Ischemic Stroke

Each year there are approximately 15M strokes that occur globally with 700,00 strokes occurring in the U.S. alone. Approximately 85% of all strokes are ischemic strokes, which occur when a blood clot blocks blood flow to the brain.

Currently, medication treatments for ischemic stroke are primarily limited to Tissue Plasminogen Activator ("TPA") or blood thinners. However, these treatments are stroke type specific and cannot be given until the patient has received a CT scan to determine if the stroke is ischemic or haemorrhagic. Patients being treated with TPA must receive the drug within 3 hours of the injury. As a result, only 5% of stroke patients receive TPA.

Additional treatment options involve surgical intervention such as catheter embolectomy and decompressive craniotomy.

Based on its preclinical data research, Algernon plans to test DMT in the clinic in patients as soon as possible after the stroke injury occurs. If it is established in the Company's preclinical research phase that DMT can be used to treat both haemorrhagic and ischemic stroke, the patient will not have to wait for a CT scan and treatment can begin immediately, possibly while being transported to the hospital.

Algernon's preclinical research is designed to help establish the optimal treatment period duration for DMT as well as the clinically effective sub-hallucinogenic dose.

2. Post-Stroke Rehabilitation

Eighty five percent of stroke survivors will end up with from some form of disability after having suffered a stroke. Intensive physical rehabilitation has been shown by researchers to improve function and reduce long-term disability.

While Algernon will investigate DMT to treat a patient as quickly as possible after the stroke occurs, it will also investigate the potential of the drug as a treatment during the rehabilitative process. Rehabilitation therapy, which includes motor-skill exercises, mobility training and range-of-motion therapy, and can begin as soon as 24 to 48 hours after the stroke has occurred.

One specific type of rehabilitation therapy, previously referenced, is called CIMT. It is focused on improving upper extremity function in stroke patients and involves intensive training of the weaker arm while restricting the use of the stronger arm.

Algernon will investigate DMT in preclinical animal models of CIMT for the promotion of neurogenesis and structural and functional neural plasticity during various time periods after the stroke has occurred. If the final data is positive, the Company will move DMT into a separate clinical trial to test for its efficacy as a post stroke rehabilitation adjunctive treatment.

Pathway to Clinical Trials

1. Pre-IND U.S. FDA & CTA - Health Canada

Based on historical data showing that several DMT Phase 1 studies have already been conducted, the Company believes that it will be able to use this data to seek approval to begin its own Phase 1 study without having to complete certain toxicology work.

In order to confirm its regulatory plans, Algernon's goal is preparing to submit a pre-IND (Investigational New Drug) meeting request with the U.S. FDA in calendar Q1 of 2021, and to present all elements of the Company's clinical program design in order to receive their guidance and advice.

The Company also intends to submit a Clinical Trial Application (CTA) to Health Canada in order to obtain additional insight and options for the Company's planned clinical research program.

2. U.S. FDA Breakthrough Therapy Designation

Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).

The Company plans to file an application with the U.S. FDA for a Breakthrough Therapy designation as soon as possible.

Algernon Stroke Program Consultants

The Company has engaged a number of global experts in the areas of DMT research and stroke including:

DMT

- **Dr. Rick Strassman MD**

  Dr. Strassman is a native of Los Angeles, and obtained his undergraduate degree in Biological Sciences from Stanford University, and his medical degree from Albert Einstein College of Medicine of Yeshiva University. His book *DMT: The Spirit Molecule* (2001) has sold 250,000 copies, been translated into 12 languages, and is the basis of a successful independent documentary that he co-produced. He is currently Clinical Associate Professor of Psychiatry at the UNM School of Medicine. He trained in general psychiatry at UC Davis in Sacramento and took a clinical psychopharmacology research fellowship at UC San Diego. Joining the faculty at the University of New Mexico School of Medicine in 1984, his clinical research with melatonin discovered its first known function in humans.

  Between 1990-1995 he performed the first new US clinical research with psychedelic drugs in a generation. His studies involved DMT, and to a lesser extent psilocybin, and received federal and private funding. From 1995-2008 he practiced general psychiatry in community mental health and the private sector. He has authored or co-authored nearly 50 peer-reviewed papers, has served as guest editor and reviewer for numerous scientific journals, and consulted to various government, non-profit, and for-profit entities.

- **Dr. David Nutt DM, FRCP, FRCPSYCH, FSB, FMEDSCI**

  Dr. Nutt is currently an Edmund J. Safra Professor of Neuropsychopharmacology and Head of the Centre for Neuropsychopharmacology in the Division of Brain Science, Department of Medicine, Hammersmith Hospital, Imperial College London. He is also visiting professor at the Open University in the UK and Maastricht University in the Netherlands.

  Dr. Nutt is also Chair of the charity DrugScience (formally the Independent Scientific Committee on Drugs (ISCD). He has been President of major national and international organisations: the British Neuroscience Association, the British Association for Psychopharmacology, the European Brain Council and the European College of Neuropsychopharmacology. In recognition of his research success he has been made a Fellow of the Royal Colleges of Physicians, of Psychiatrists and of the Academy of Medical Sciences. He is also the UK Director of the European Certificate and Masters in Affective Disorders Courses and a member of the International Centre for Science in Drug Policy. He has edited the Journal of Psychopharmacology for over twenty-five years and acts as the psychiatry drugs advisor to the British National Formulary. He has published over 500 original research papers, a similar number of reviews and books chapters, eight government reports on drugs and 31 books including one for the general public *Drugs Without the Hot Air*, which won the Transmission book prize in 2014. He was the clinical scientific lead on the 2004/5 UK Government Foresight initiative “Brain science, addiction and drugs” that provided a 25-year vision for this area of science and public policy.

Stroke

- **Dr. Dennis Choi MD, PhD**

  Dr. Choi is Professor of Neurology at Stony Brook University, having previously chaired that department and served as Director of the Neurosciences Institute there. Other prior positions have included Director of the Brain Science Institute at the Korea Institute of Science and Technology, Vice President for Academic Health Affairs at Emory University, Executive Vice President for Neurosciences at Merck Research Labs, and Head of Neurology at Washington University Medical School. Dr. Choi received his M.D. from the Harvard-MIT Health Sciences and Technology Program, as well as a Ph.D. in pharmacology and neurology residency training at Harvard. A fellow of the American Association for the Advancement of Science and a member of the National Academy of Medicine, he has served previously as President of the Society for Neuroscience, Vice-President of the American Neurological Association, and chairman of the U.S./Canada Regional Committee of the International Brain Research Organization.

  Dr. Choi has been a member of the Board on Life Sciences of the National Academy of Sciences; the Nervous System Drugs Advisory Committee to the U.S. Food & Drug Administration; and Councils for the National Institute of Neurological Disorders and Stroke, the National Institute on Aging, the Winter Conference for Brain Research, the International Society for Cerebral Blood Flow and Metabolism, and the Neurotrauma Society; as well as the advisory boards of multiple companies and non-profit disease

foundations. He was a founding co-editor-in-chief of the research journal, *Neurobiology of Disease* (Elsevier). He has been a pioneer in developing the field of neuroprotection, identifying mechanisms responsible for nervous system injury after acute insults and developing therapeutic countermeasures.

Manufacturing

Instead of trying to harvest DMT from natural sources, a process which can result in issues with purity and supply, synthetically produced DMT will provide a source of stable and trusted drug substance and will enable the supply of large quantities for all Algernon research purposes as well as clinical needs going forward, on a global scale.

Algernon is currently engaged in discussions with a Health Canada and U.S. FDA approved drug manufacturing company that has the experience and required licensure for the manufacturing and handling of DMT.

CRO's

Algernon has retained CRO Clinical Development Solutions ("CDS"), to support all aspects of the investigational brochure, study protocol and Pre-IND and IND application with the U.S. FDA as well as the CTA with Health Canada. CDS will provide high-level oversight and management of all clinical trials.

The Company has also retained Novotech to conduct a feasibility study for Algernon to conduct all or part of its DMT stroke clinical research program in Australia. The Company has currently engaged Novotech for its Phase 2 clinical study for idiopathic pulmonary fibrosis and chronic cough as well as COVID-19. Australia is a favoured country for clinical research because of its government supported 43.5% refundable tax credit program.

Algernon is also exploring conducting its DMT clinical research program in other countries as well.

About Algernon Pharmaceuticals Inc.

Algernon is a drug re-purposing company that investigates safe, already approved drugs, including naturally occurring compounds, for new disease applications, moving them efficiently and safely into new human trials, developing new formulations and seeking new regulatory approvals in global markets. Algernon specifically investigates compounds that have never been approved in the U.S. or Europe to avoid off label prescription writing.

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