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Algernon Pharmaceuticals Announces Plans for a 180 Patient Phase 2b Chronic Cough Study of Ifenprodil

Ifenprodil Represents a Novel First-in-Class Potential Treatment for Chronic Cough

VANCOUVER, British Columbia, Jan. 09, 2023 (GLOBE NEWSWIRE) -- Algernon Pharmaceuticals Inc. (the "Company" or "AGN Pharma") (CSE: AGN) (FRANKFURT: AGW0) (OTCQB: AGNPF), a Canadian clinical stage pharmaceutical development company, is pleased to announce that it is planning a 180 patient, 90-day Phase 2b clinical study of NP-120 ("Ifenprodil") for chronic cough to begin in Q3 of 2023. Ifenprodil is an N-methyl-D-aspartate (NMDA) receptor antagonist specifically targeting the NMDA-type subunit 2B (GluN2B), which prevents glutamate signaling. Ifenprodil represents a novel first-in-class potential treatment for chronic cough and is thought to interfere with central signalling in the brain, suppressing the urge to cough.

"I am very pleased Algernon has decided to conduct a stand-alone, Phase 2b study for cough," said Dr. Jacky Smith, Professor of Respiratory Medicine at the University of Manchester, and an Honorary Consultant at Manchester University NHS Foundation Trust. "I recommended, based on Algernon's encouraging Phase 2a clinical data, that the Company further explore Ifenprodil in chronic cough in a well-designed, sufficiently powered study that will give clear answers on the potential efficacy of the drug in this population."

In addition to being Algernon's lead chronic cough advisor, Dr. Smith is also a consultant to Merck & Co. and Bellus Health, both of which are pursuing a drug for the indication of chronic cough.

The decision to advance the study is based on positive data previously reported on July 28, 2022, from the Company's Phase 2a study of Idiopathic Pulmonary Fibrosis (IPF) and chronic cough, where Ifenprodil showed a significant improvement in mean objective 24-hour and waking cough counts in patients after 4 and 12 weeks. Patients with IPF are usually excluded from trials in refractory chronic cough, and cough in this population is regarded as extremely difficult to treat.

The analysis showed that:

- The geometric mean 24-hour cough counts were reduced by 32.0% at 4 weeks ($p = 0.023$) and 39.5% at 12 weeks ($p = 0.001$) compared to baseline
- The geometric mean awake cough counts were reduced by 30.2% at 4 weeks ($p = 0.038$) and 37.4% at 12 weeks ($p = 0.002$) compared to baseline

Algernon previously announced on January 14, 2022, that it had received positive feedback

from the U.S. Food and Drug Administration (U.S. FDA) at its pre-Investigational New Drug (pre-IND) meeting for its investigation of Ifenprodil solely for the treatment of chronic cough. The Company has since engaged in further discussions with the U.S. FDA, and plans to file an investigational new drug (IND) application shortly.

While the Company originally planned to focus on IPF in a Phase 2b study, Algernon has now decided to pursue a chronic cough study first, and to delay planning its IPF Phase 2b study for Ifenprodil until a later date.

Study Design

The planned study design will include the following elements:

- Multinational, three-arm, randomized, double-blind, placebo-controlled trial to evaluate NP-120 in approximately 180 patients.
- Patients will be randomized 1:1:1 to receive NP-120 (20mg TID) or NP-120 (40mg TID), or placebo for 12 weeks.
- The primary endpoint will be the reduction in geometric mean 24-hr cough count over 12 weeks compared to placebo.
- Secondary endpoints will include safety, tolerability and patient-reported quality-of-life measures.

"The design of Phase 2 studies in chronic cough have been validated in trials conducted by Merck & Co and Bellus Health," said Christopher J. Moreau CEO of Algernon Pharmaceuticals. "By mirroring the design of those studies, Algernon will have a direct benchmark for comparison and, if successful, a clear regulatory path for Ifenprodil for the treatment of chronic cough."

Chronic Cough Market

According to Data Bridge Market Research analyses, the global chronic cough market was valued at USD $6.15B in 2021, and it will grow up to USD $11.38B by 2029.

Merck & Co. obtained the rights to Gefapixant, a P2X3 receptor antagonist, as the lead asset in the acquisition of Afferent Pharmaceuticals in 2016. At the time, Gefapixant had interim data from a Phase 2b dose-escalation study in refractory chronic cough. The deal was worth up to USD $1.25B.

Bellus Health which is advancing its own novel P2X3 receptor antagonist, BLU-5937, has a market cap of over USD $1.4B.

About Chronic Cough

Chronic cough is defined as a cough lasting for more than eight weeks in duration and in the United States cough continues to be one of the most common reasons that adults consult medical doctors. Some cases of chronic cough are so debilitating that quality of life is severely impacted leading to depression, anxiety, urinary incontinence, dysphonia, sleep interruption, vomiting, and even rib fractures further adding to the decay in socio-familial

dynamics.

Chronic cough is believed to be the result of a hypersensitivity of the cough reflex within the neuronal circuitry that governs the urge to cough, wherein one or more aspects that regulate cough are over-active to stimulus, triggering a cough at abnormal levels. Trials of cough suppressants (Antitussives) have shown differences in response that may reflect differing pathological processes driving cough in different patients. Experimental Antitussives often only engage a single receptor, while the overall cough response is governed by multiple receptors triggered by a large variety of stimuli. A compound acting centrally where all peripheral messages are sent and coordinated may achieve a better outcome than what has been achieved in clinical trials.

About NP-120 (Ifenprodil)

Ifenprodil selectively inhibits N-methyl-D-aspartate (NMDA) receptors containing the NR2B subunit. NMDA receptors are ion-channels found within the central and peripheral nervous system, including the area of the brain responsible for coordinating the cough reflex. They are highly implicated in events such as neuronal plasticity (strengthening of neural pathways) and excitotoxicity (neurotoxic cascade resulting in neuron death).

By inhibiting NMDA receptors, Ifenprodil can diminish excitability of neurons and prevent the relaying of information along neuronal circuitry, including the cough reflex. Ifenprodil may also inhibit the neuroplastic enhancement of central and peripheral cough response neurons.

About Algernon Pharmaceuticals Inc.

Algernon Pharmaceuticals is a Canadian clinical stage drug development and repurposing company investigating multiple drugs for unmet global medical needs. Algernon Pharmaceuticals has active research programs for IPF with chronic cough, and chronic kidney disease, and is the parent company of a newly created private subsidiary called Algernon NeuroScience, that is advancing a psychedelic program investigating a proprietary form of psychedelic DMT for stroke.

CONTACT INFORMATION

Christopher J. Moreau
CEO
Algernon Pharmaceuticals Inc.
604.398.4175 ext 701
info@algernonpharmaceuticals.com
investors@algernonpharmaceuticals.com
www.algernonpharmaceuticals.com.

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