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Algernon Pharmaceuticals Hits Co-Primary Endpoint in its Phase 2 Study of Ifenprodil for Idiopathic Pulmonary Fibrosis and Chronic Cough

VANCOUVER, British Columbia, July 18, 2022 (GLOBE NEWSWIRE) -- Algernon Pharmaceuticals Inc. (the "Company" or "Algernon") (CSE: AGN) (FRANKFURT: AGW0) (OTCQB: AGNPF) a clinical stage Canadian pharmaceutical development company, is pleased to announce positive topline data showing that it has met the co-primary endpoint in its Phase 2 proof of concept study evaluating NP-120 ("Ifenprodil") for the potential treatment of idiopathic pulmonary fibrosis ("IPF") and chronic cough. In the study, 65% of patients had stable or improved forced vital capacity ("FVC") over the 12-week treatment period with statistical significance when compared to an anticipated placebo effect of 40%. FVC is the amount of air that can be forcibly exhaled from one's lungs after taking the deepest breath possible.

Ifenprodil is an N-methyl-D-aspartate (NMDA) receptor antagonist specifically targeting the NMDA-type subunit 2B (GluN2B), which prevents glutamate signalling. Ifenprodil represents a novel first in class treatment for both IPF and chronic cough.

IPF Data Set

To understand the potential efficacy for Ifenprodil in IPF patients, lung function in this trial was measured by FVC (a best-efforts measurement) which was taken for each patient at baseline, and then again at 12 weeks. Patients whose FVC declined were classified as non-responders, while those whose FVC improved or remained stable were classified as responders. The primary endpoint of the IPF part of the study was the proportion of patients who responded.

Of the 20 patients who enrolled, 13 (65%) had stable or improved FVC over the 12-week treatment period with statistical significance when compared to an anticipated placebo effect of 40% (p=.0225, 95% CI 40.8 to 84.6%, all numbers are Intent-to-Treat analysis). Importantly, key opinion leaders advising the company, as well as historical data on previously conducted IPF clinical studies[(1)], indicated that approximately 30-40% of patients IPF patients would experience no decline in FVC if they were dosed with a placebo over the 12-week period, demonstrating that Ifenprodil showed promising initial IPF efficacy in this trial.

The Company also reports trends to reduction in many of the serum markers that were tested including proC3, C3M, C6M, reC1M, proC8 and ELP-3, although the data did not reach statistical significance. Elevation of these markers has been associated with increased mortality and risk of disease progression in previous research studies.

“The IPF data looks quite good,” said Dr. Martin Kolb, professor of respirology at McMaster University and global expert on IPF. “I was very surprised to see the data achieve statistical significance with such a small study size, when you consider the original goal of the study was to try to identify a signal. As a result, I am confident that the Company should begin planning a sufficiently powered Phase 2b study to investigate Ifenprodil as a possible new treatment for IPF patients, including those who have associated cough.”

Chronic Cough Data Set

For the chronic cough part of the study’s primary endpoint, 30% of subjects achieved the endpoint of a 50% reduction in the average number of coughs per hour over 24 hours from baseline to week 12. While this primary cough study endpoint did not achieve statistical significance when compared to an anticipated placebo effect of 25%, the secondary endpoint of actual changes (reduction) in cough counts did. Specifically, subjects experienced a 24% relative reduction from baseline in mean cough count, and a 38% relative reduction from baseline in median cough count in their 24-hour cough count per hour at week 12 (p=0.0344). In addition, 75% of subjects saw improvements in their cough over 12 weeks.

This data shows that while Ifenprodil didn't achieve the more stringent primary endpoint parameter on cough, there is a definite signal (effect) when comparing cough counts directly to their baseline measurement. Furthermore, in contrast with recent studies on cough drugs targeting purinergic receptors, the observed effect may not be dependent on a subject’s baseline cough count; in a subgroup analysis, subjects with baseline cough counts below the median for the study appeared to achieve similar reductions in relative cough count to those with baseline counts above the median.

“These data are quite compelling,” said Dr. Jacky Smith, Professor of Respiratory Medicine at the University of Manchester, and an Honorary Consultant at Manchester University NHS Foundation Trust. “Although the primary cough endpoint does not reach statistical significance, the reductions in cough counts, particularly the median cough counts, are suggestive of a beneficial effect. Furthermore, the choice of a 25% response rate as a comparator may understate the benefit. Existing IPF therapies have little to no effect on cough, and so coupled with the results in IPF seen in this trial, there is great reason for optimism. I am working with the Company to further analyze the data and encourage them to continue to study the effects on cough as development of this drug continues.”

Safety Data

The results also show that Ifenprodil’s safety profile in this trial was consistent with findings from previous studies of the drug, with no new safety signals observed. 45% of subjects experienced at least one treatment-emergent adverse events (TEAE), most of which were mild in intensity. The most common TEAE’s were gastrointestinal disorders (25%) and decreased appetite (10%). One participant withdrew from the study due to a hepatic neuroendocrine tumour unrelated to Ifenprodil, that resulted in death. Although Ifenprodil has been used in Japan for decades to treat vertigo, this is the first study in an IPF population, and so the Company is pleased to report that no new safety concerns were identified.

Full Data Set

The Company expects to receive the full data set from the study in August 2022 and will present the full results of the study at the 21st International Colloquium on Lung and Airway Fibrosis in Reykjavik, Iceland in October 2022.

“Simply put, the IPF data is better than we could have imagined,” said Christopher J. Moreau, CEO of Algernon. “The outlook for patients with IPF remains dismal, with 50% mortality expected within 3-4 years and new drugs are desperately needed. Also, the IPF market size is projected to reach $4.2 billion by 2030[(2)], so it is a very commercially appealing indication to be advancing a new drug for. While the cough data is also promising, we will wait until we have the full data set before making any final decisions on pursuing both IPF and chronic cough in separate Phase 2b clinical studies, or focussing on just IPF patients with associated cough.”

U.S FDA pre-IND

Based on the positive data, the Company plans to file a pre-IND application with the U.S. FDA for a Phase 2b IPF study. The current plan would be to switch to a new once-a-day formulation of Ifenprodil from the 3-times daily dosing currently being used. The Phase 2b study will also have multiple arms, multiple doses, would be placebo controlled and would be double blinded and randomized.

For chronic cough, the Company has already filed a pre-IND application with the U.S. FDA and has announced that it has received positive feedback.

The Company will take additional time to review the full data set before a decision is made to pursue an independent Phase 2b study of chronic cough or to focus on Ifenprodil as a potential new IPF drug that also reduces cough for those patients that are suffering from both.

U.S Orphan Indication and Breakthrough Therapy

IPF is also classified as an orphan disease indication and as such, any new approved drugs are provided 7-year and 10-year market exclusivity in both the U.S and Europe, respectively. The Company plans to file for an orphan designation with the U.S FDA for Ifenprodil and IPF shortly.

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

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).

Ifenprodil Patents

The Company also recently announced that it has been issued a patent from the Canadian Intellectual Property Office, No. 3101853, for the treatment of interstitial lung disease with Ifenprodil, entitled “Compositions and Methods for Treating Idiopathic Pulmonary Fibrosis.”

The invention claims treating interstitial lung disease, including IPF, with Ifenprodil. The base

claims of the patent will be valid through 2040, excluding any patent term adjustments or extensions which may provide additional protection. The Company also has active patent applications for Ifenprodil for the same compositions and methods in the U.S., Europe, China and Japan.

About Ifenprodil

Ifenprodil is an N-methyl-D-aspartate (NMDA) receptor antagonist specifically targeting the NMDA-type subunit 2B (GluN2B). Ifenprodil prevents glutamate signalling. The NMDA receptor is found on many tissues including lung cells, T-cells, and neutrophils.

https://erj.ersjournals.com/content/55/5/1902151(1)
https://www.astuteanalytica.com/industry-report/idiopathic-pulmonary-fibrosis-market(2)

About Algernon Pharmaceuticals Inc.

Algernon is a drug re-purposing company that investigates safe, already approved drugs 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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Source: Algernon Pharmaceuticals