July 20, 2022

Adial Pharmaceuticals Announces Topline Results For Onward™ Phase 3 Trial for AD04 in Patients with Alcohol Use Disorder

AD04 achieved statistically significant mean reduction in heavy drinking days among pre-specified group of heavy drinkers, compared to placebo, with an approximately 79% reduction from baseline drinking

AD04 demonstrated statistically significant difference in AUD severity, as compared to placebo, with an 84% decrease in the number of heavy drinking patients meeting the criteria for AUD diagnosis

Company plans to submit ONWARD results to both European and U.S. regulatory agencies

Conference call to be held today at 1:00 p.m. Eastern Time

CHARLOTTESVILLE, Va., July 20, 2022 (GLOBE NEWSWIRE) -- **Adial Pharmaceuticals, Inc. (NASDAQ: ADIL; ADILW)** ("Adial" or the "Company"), a clinical-stage biopharmaceutical company focused on developing therapies for the treatment and prevention of addiction and related disorders, today announced successful results from the Company's ONWARD trial, a Phase 3 clinical study to evaluate the efficacy, safety and tolerability of AD04 in patients with Alcohol Use Disorder ("AUD") and selected polymorphisms in the serotonin transporter and receptor genes.

AD04 achieved statistically significant mean reduction in heavy drinking days among the pre-specified group of "heavy drinkers" (defined below). AD04 also showed safety and tolerability that compared favorably to placebo. Adial intends to share the results of the ONWARD trial with the relevant health authorities to discuss the appropriate next steps towards the expeditious development of AD04 and to seek product approval.

Highlights of topline ONWARD data:

- AD04 patients, compared with placebo patients, achieved a statistically significant reduction from baseline at month six in heavy drinking days for the pre-specified patient group of heavy drinkers (avg. <10 drinks per drinking day at baseline; p=0.03), which accounted for approximately two-thirds of the trial population. A similar trend was seen in the combined month five and six analysis in the reduction from baseline (p =0.07). Notably, in the last month of the trial, AD04 heavy drinking patients had a mean reduction of approximately 79% in heavy drinking compared with baseline.
- AD04 patients, compared with placebo patients, showed a trend in the reduction from

baseline at month six in heavy drinking days for the combined trial population of heavy and very heavy drinkers (p=NS), which was influenced by the high placebo response among very heavy drinkers (avg. ≥10 drinks per drinking day at baseline), due to both the AD04 and placebo groups reducing mean heavy drinking days by more than 50%. A similar, non-statistically significant trend was seen in the combined months five and six analysis in the reduction from baseline, which was the pre-specified primary efficacy analysis.

- At conclusion of the trial, compared with placebo patients, AD04 patients in the heavy drinking group had an overall significant difference in the severity of their AUD diagnosis (p=0.04) under the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). For the group of those who no longer meet AUD criteria (<2 symptoms), the comparisons were 27.4% vs. 14.9% (i.e., an 84% decrease), of AD04 and placebo patients, respectively. These data underscore the clinical relevance of the findings that heavy drinking AUD patients that receive AD04 appear more likely to recover from the disease by the end of the treatment regimen.
- Based on the levels of alcohol consumption reported in a meta-analysis of 83 prospective studies in primary care screening for those with AUD (Wood, et. al., Lancet 2018), the Company estimates that a majority of potential patients for AD04 would fall under the pre-specified group of heavy drinkers. This finding underscores the potential broad applicability of the results to general practice and that they could be the basis for potential regulatory approvals.

Additionally, and consistent with the Phase 2b trial, AD04 had a safety and tolerability profile that was similar to placebo:

- Serious Adverse Events (SAEs)
  - No SAEs were determined to be related to AD04 treatment.
  - More SAEs were reported in the placebo group compared with the AD04 group (7 on placebo vs. 3 on AD04).
  - There were two cardiac events in placebo group and none in the AD04 group.
- Side effects/Adverse Events (AEs)
  - The AE profiles between AD04 and placebo were similar.
  - AEs reported with a frequency of 5% or more of patients in either group were: headache (11% on placebo, 12% on AD04), insomnia (3% on placebo, 7% on AD04), blood magnesium decreased (5% on placebo, 6% on AD04), and fatigue (3% on placebo, 6% on AD04). All of the above AE's were reported as mild to moderate.
  - Importantly, in the overall category of cardiac disorders, patients on placebo showed a greater number of adverse events relative to AD04 (7% on placebo, 4% on AD04), in addition to greater number of cardiac SAEs in the placebo group as reported above.

William Stilley, Chief Executive Officer of Adial, commenting on the trial results, said, "Alcohol Use Disorder is an unmet medical need that affects tens of millions of people each year, and, based on the strength of these ONWARD results in heavy drinking patients that have the target genetics, and the fact that AD04 demonstrated an exceptional safety profile, and was well-tolerated during the trial, we intend to advance AD04. We will work with regulatory authorities in Europe and the U.S. to achieve this goal. We also plan to explore strategic partnerships."

Professor Hannu E.R. Alho, Emeritus Professor of Addiction Medicine at the University of Helsinki and Principal Investigator for the ONWARD trial, stated, “These study results may provide hope to millions of people worldwide suffering from AUD, as well to the families of those impacted by this devastating disease. Among heavy drinkers, which make up the majority of my practice, we saw a clear and statistically significant reduction in heavy drinking days for those patients receiving AD04 versus placebo. These results demonstrate the effectiveness of AD04 for heavy drinker AUD patients.”

Professor. Dr. Bankole Johnson, Chief Medical Officer of Adial, said, “It has been my life mission to develop new therapies that provide patients with a means to either curb the impulse to drink, or abstain from alcohol entirely. AUD accounts for more than 5% of deaths worldwide and is the number one indicator of death for men and women ages 15 to 49, the prime of their lives. The ONWARD study reinforces that AUD is a multi-factorial disease with a diverse set of neurobiological components. The ONWARD data appears to support our earlier findings that AD04 is a genetically targeted medical treatment addressing the biology of AUD. We believe our finding that AD04 appears as safe as placebo should increase its acceptability in general practice and eventually lead to widespread adoption of AD04 for treatment of AUD.”

The Company is planning further communication regarding the ONWARD results and its future plans for product development and regulatory interactions.

Conference Call

The Company will host a conference call at 1:00 P.M. Eastern Time on Wednesday, July 20, 2022 to discuss the clinical results in more detail.

The conference call will be available via telephone by dialing toll free 888-506-0062 for U.S. callers or +1 973-528-0011 for international callers and by entering the access code: 810744. A webcast of the call may be accessed a t https://www.webcaster4.com/Webcast/Page/2463/46199 or on the Company’s website at https://www.adial.com/newsroom/#section=adial-events.

A webcast replay of the call will be available on the Company’s Investor Relations Section of the website (www.ir.adial.com) through July 20, 2023. An audio replay of the call will be available through August 3, 2022 and can be accessed by dialing 877-481-4010 for U.S callers or +1 919-882-2331 for international callers and by entering the access code: 46199.

About the ONWARD™ Trial

The ONWARD Phase 3 clinical trial was a 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel group, clinical study to evaluate the efficacy, safety and tolerability of AD04 in patients with Alcohol Use Disorder and selected polymorphisms in the serotonin transporter and receptor genes. Patients were genetically screened prior to enrollment in ONWARD so that only genetically positive patients were enrolled, and patients were stratified by the severity of drinking into heavy drinkers and very heavy drinkers (determined by whether they averaged less than ten, or greater than or equal to ten drinks per drinking day, respectively, prior to enrollment). Approximately, two-thirds of the patients in the ONWARD trial were in the heavy drinking group and one-third in the very heavy drinker group.

ONWARD was conducted in 25 clinical sites in six countries in Scandinavia and Central and Eastern Europe (Sweden, Finland, Poland, Latvia, Bulgaria and Croatia). The principal investigator was Professor Hannu E.R. Alho, Emeritus Professor of Addiction Medicine at the University of Helsinki.

About Alcohol Use Disorder

According to an article in the widely respected publication The Lancet, alcohol is the number one cause of death globally among both men and women ages 15 to 49 years. In the United States alone, approximately 35 million people have AUD resulting in significant health, social and financial costs (NIAAA Alcohol Facts & Statistics). AUD contributes to over 200 different diseases, and 10% of children live with a person that has an alcohol problem. According to the American Society of Clinical Oncologists, 5-6% of new cancers and cancer deaths globally are directly attributable to alcohol. The Centers for Disease Control (CDC) has reported that AUD costs the U.S. economy about $250 billion annually, with heavy drinking accounting for greater than 75% of the social and health related costs. In addition, according to the NIAAA, the problem in the United States appears to be growing with an approximately 50% increase in AUD prevalence between 2002 and 2013.

Despite the high prevalence and high costs, according to an article in the JAMA 2015 publication, only 7.7% of patients (i.e., approximately 2.7 million people) with AUD are estimated to have been treated in any way and only 3.6% by a physician (i.e., approximately 1.3 million people). The most common treatments for AUD are directed at achieving abstinence, and typical treatments include psychological and social interventions. Most therapies require abstinence even prior to initiating therapy. Abstinence requires dramatic lifestyle changes often with serious work and social consequences. Significant side effects of current pharmacologic therapies include mental side effects, such as psychiatric disorders and depressive symptoms and physical side effects, such as nausea, dizziness, vomiting, abdominal pain, arthritis and joint fitness. These problems with the currently available therapies appear to limit the willingness of people with AUD to seek treatment and then to limit compliance with treatment requirements and, therefore, the ultimate results for many people attempting currently available therapies.

About Adial Pharmaceuticals, Inc.

Adial Pharmaceuticals is a clinical-stage biopharmaceutical company focused on the development of treatments for addictions. The Company's lead investigational new drug product, AD04, is a genetically targeted, serotonin-3 receptor antagonist, therapeutic agent for the treatment of Alcohol Use Disorder (AUD) in heavy drinking patients and was recently investigated in the Company's ONWARD™ pivotal Phase 3 clinical trial for the potential treatment of AUD in subjects with certain target genotypes (estimated to be approximately one-third of the AUD population) identified using the Company's proprietary companion diagnostic genetic test. ONWARD showed promising results in reducing heavy drinking in heavy drinking patients, and no overt safety or tolerability concerns. AD04 is also believed to have the potential to treat other addictive disorders such as Opioid Use Disorder, gambling, and obesity. The Company is also developing adenosine analogs for the treatment of pain and other disorders. Additional information is available at www.adial.com.

Forward Looking Statements

This communication contains certain "forward-looking statements" within the meaning of the U.S. federal securities laws. Such statements are based upon various facts and derived utilizing numerous important assumptions and are subject to known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Statements preceded by, followed by or that otherwise include the words "believes," "expects," "anticipates," "intends," "projects," "estimates," "plans" and similar expressions or future or conditional verbs such as "will," "should," "would," "may" and "could" are generally forward-looking in nature and not historical facts, although not all forward-looking statements include the foregoing. The forward-looking statements include statements regarding sharing the results of the ONWARD trial with the relevant health authorities to discuss the appropriate next steps towards the expeditious development of AD04 and to seek product approval, estimates that a majority of potential patients for AD04 would fall under the pre-specified group of heavy drinkers, the potential broad applicability of the results to general practice and that they could be the basis for potential regulatory approvals, intent to advance AD04 and working with regulatory authorities in Europe and the U.S. to achieve this goal, plans to explore strategic partnerships, the study results providing hope to millions of people worldwide suffering from AUD, AD04 appearing as safe as placebo increasing its acceptability in general practice and eventually lead to widespread adoption of AD04 for treatment of AUD, further communication regarding the ONWARD results and future plans for product development and regulatory interactions and the potential of AD04 to treat other addictive disorders such as opioid use disorder, gambling, and obesity. Any forward-looking statements included herein reflect our current views, and they involve certain risks and uncertainties, including, among others, the ability of AD04 to be approved by regulatory authorities for treatment of AUD, our ability to commercialize product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to our ability to promote or commercialize our product candidates for specific indications, acceptance of its product candidates in the marketplace and the successful development, marketing or sale of products, our ability to maintain our license agreements, the continued maintenance and growth of our patent estate, our ability to establish and maintain collaborations, our ability to obtain or maintain the capital or grants necessary to fund its research and development activities, and our ability to retain our key employees or maintain our Nasdaq listing. These risks should not be construed as exhaustive and should be read together with the other cautionary statement included in our Annual Report on Form 10-K for the year ended December 31, 2021, subsequent Quarterly Reports on Form 10-Q and current reports on Form 8-K filed with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was initially made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise, unless required by law.

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