atai Life Sciences Announces Positive Preliminary Results from Phase 1b Trial of VLS-01 (Buccal Film DMT)

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- *VLS-01 is designed to induce a short psychedelic experience, allowing for a total in-clinic treatment of 2-hours, consistent with an established commercial paradigm in interventional psychiatry*

- *VLS-01 reached peak plasma concentration within 30-45 minutes and was shown to induce a short psychedelic experience, with subjective effects generally resolving within 90-120 minutes*

- *VLS-01 demonstrated a favorable safety profile and was well tolerated, with all adverse events classified as either mild or moderate, and most resolving on the day of dosing*

- *atai expects to initiate a randomized, double-blind, placebo-controlled Phase 2 study of VLS-01 to assess the efficacy, safety and durability of response of repeated doses in patients with treatment-resistant depression around year-end 2024*

NEW YORK and BERLIN, Aug. 13, 2024 (GLOBE NEWSWIRE) -- atai Life Sciences (NASDAQ: ATAI) ("atai" or "Company"), a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders, today announced positive preliminary results from the Phase 1b trial of VLS-01, its proprietary oral transmucosal film formulation of *N,N*-dimethyltryptamine (DMT) that is applied to the buccal surface.

The Phase 1b trial was designed to evaluate the relative safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of VLS-01 compared to intravenous (IV) DMT. The single center, open-label study enrolled a total of 17 healthy participants, each of whom received a single dose of IV DMT followed by 3 different doses of VLS-01 buccal film—20mg (N=8), 60mg (N=6), 120mg (N=14) or 160mg (N=16)—with a 28-day washout window between administrations.

Key takeaways:

- Peak plasma concentrations (Cmax) were dose-proportional and comparable between the higher VLS-01 buccal film doses (120mg and 160mg) and the 30mg IV DMT dose; peak plasma concentrations were achieved within 30-45 minutes (Tmax).
- Dose-dependent and robust subjective effects were seen at the 120mg and 160mg doses.
- In the 120mg dose cohort:
  - 13/14 participants achieved Subjective Intensity Rating Scale (SIRS) scores greater than seven out of ten.
  - Subjective effects, assessed with the SIRS, were fully resolved by 120 minutes.
  - Participants reported that the experience was 'psychologically meaningful' with 'increased levels of self-reflection'.

Safety and tolerability:

- VLS-01 demonstrated a favorable safety profile and was well tolerated, with all adverse events classified as either mild or moderate, and most resolving on the day of dosing.
- The most common treatment-emergent adverse events (TEAEs) were headache, dissociation, euphoric mood and nausea.
- No TEAEs of vomiting or local irritation were noted at doses of 120mg or lower, and only 1 subject out of 14 (7%) reported nausea at the 120mg dose.
- There were no observed adverse events related to blood pressure, heart rate or suicidality.

"We're delighted with the positive results from the VLS-01 Phase 1b study, which further support its potential as a promising therapeutic option for the 100 million people worldwide suffering from treatment-resistant depression," stated Dr. Srinivas Rao, Co-Chief Executive Officer and Co-founder of atai.

"In this trial, the 120mg dose was found to strike a balance between psychedelic effect intensity and safety as well as tolerability. These encouraging findings, if replicated in Phase 2, suggest that VLS-01 could become a best-in-class treatment for TRD, one that offers a well-tolerated, convenient oral dosing and a short psychedelic experience that fits into the two-hour in-clinic commercial paradigm established within interventional psychiatry. These Phase 1b results lay a strong foundation for our Phase 2 trial in patients with treatment-resistant depression, which is set to begin around year-end."

Based on the positive results from the Phase 1b trial, the Company plans to initiate a randomized, double-blind, placebo-controlled Phase 2 study (NCT06524830) to assess the safety, efficacy and durability of response of repeated doses of VLS-01 in patients

with treatment-resistant depression (TRD). The Phase 2 trial will consist of two treatment periods.

In the first treatment period, approximately 142 patients will be randomized 1:1 to receive a 120mg dose of VLS-01 buccal film or placebo on Day 1, followed by a second dose of the same intervention at Week 2. The primary endpoint is the change from Baseline in Montgomery-Asberg Depression Rating Scale (MADRS) total score at Week 4 and the last double-blind assessment visit will be at Week 14. The first treatment period will provide 12 weeks of durability data following two doses of VLS-01 administered in a placebo-controlled fashion.

The second treatment period starts at Week 14 and will explore the response to two different dose levels of VLS-01. Patients will be randomized 1:1 to receive a third dose of either 60mg or 120mg of VLS-01. Final safety and efficacy assessment will be conducted two weeks after administration of the third dose.

atai expects to initiate the Phase 2 trial around year-end 2024, with topline data anticipated around year-end 2025.

About VLS-01
VLS-01 (also referred to as VLS-01-BU) is a proprietary oral transmucosal film formulation of DMT applied to the buccal surface, being developed for patients living with treatment-resistant depression. Pharmacologically, DMT is a partial agonist of the 5-HT 1A/2A/2C receptors, characterized by an intrinsically short duration of psychedelic effect. Clinical evidence suggests that a single administration of intravenous (IV) DMT results in rapid-acting and durable antidepressant effects in patients with major depressive disorder. The Company's proprietary buccal film formulation is designed to eliminate the need for IV administration, provide improved PK compared to such route of administration, and maximize the therapeutic potential of a two-hour in-clinic patient visit.

About atai Life Sciences
atai is a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders and was founded as a response to the significant unmet need and lack of innovation in the mental health treatment landscape. atai is dedicated to efficiently developing innovative therapeutics to treat depression, anxiety, addiction, and other mental health disorders. By pooling resources and best practices, atai aims to responsibly accelerate the development of new medicines to achieve clinically meaningful and sustained behavioral change in mental health patients. atai's vision is to heal mental health disorders so that everyone, everywhere can live a more fulfilled life. For more information, please visit www.atai.life.

Forward-looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "could," "would," "project," "plan," "potentially," "preliminary," "likely," and the negative of these terms and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All statements contained in this press release other than statements of historical fact should be considered forward-looking statements, including without limitation our expectations and projections regarding the success, potential uses and timing of development of VLS-01 and related trials and studies, and our business strategy and plans.

Because forward-looking statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include, among others: clinical and preclinical development is uncertain, and our programs may experience delays or may never advance to clinical trials; our reliance on third parties to assist in conducting our clinical trials including failure by third parties to meet trial or testing deadlines; our reliance on qualified therapists working at third-party clinical trial sites to administer certain of our product candidates; the timing and outcome of regulatory review and/or approvals; research and development of drugs targeting the central nervous system, or CNS, is particularly difficult, and it can be difficult to predict and understand why a drug has a positive effect on some patients but not others; significant competition; obtaining, maintaining and protecting our intellectual property; restricted operating activity as a result of covenants in any financing arrangements; and operational activity. These forward-looking statements are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the risks, uncertainties, and assumptions described in our Form 10-K for the year ended December 31, 2023, filed with the Securities and Exchange Commission ("SEC") and our quarterly reports on Form 10-Q, as may be updated by other filings we file with or furnish to the SEC.

Any forward-looking statements made herein speak only as of the date of this press release. Except as required by applicable law, we undertake no obligation to update any of these forward-looking statements for any reason after the date of this press release or to conform these statements to actual results or revised expectations.

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