atai Life Sciences announces FDA Investigational New Drug (IND) Clearance for PCN-101 R-ketamine Program

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- Enables expansion of PCN-101 clinical development to the U.S.
- atai plans to initiate clinical drug-drug interaction (DDI) study in early 2022 to assess pharmacokinetics of PCN-101 when used concurrently with other drugs
- DDI trial will complement existing Phase 2a trial in treatment-resistant depression (TRD) recently initiated in Europe

NEW YORK, Jan. 12, 2022 (GLOBE NEWSWIRE) -- atai Life Sciences N.V. (Nasdaq: ATAI) (“atai”), a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders, today announced the U.S. Food and Drug Administration (FDA) has given Investigational New Drug (IND) clearance to conduct a clinical DDI study of PCN-101 (R-ketamine). atai plans to initiate the study early this year through its platform company Perception Neuroscience.

The unique properties of PCN-101 could offer a differentiated profile to currently available antidepressants and address key patient needs, including the potential of rapid action and anti-suicidal effect. Rapid onset of action is particularly important in this patient population, but frontline selective serotonin reuptake inhibitors (SSRIs) can take up to 12 weeks before providing maximal benefit, while suicidality affects as much as 30% of treatment-resistant depression (TRD) patients at least once during their lifetime.[1-3]

In preclinical animal models of depressive behavior, R-ketamine has demonstrated the potential to offer longer durability and a potentially more favorable safety and tolerability profile than S-ketamine, which could enable the potential for at-home use.[4,5] In addition, a third-party, open-label study observed a rapid, durable antidepressant response and limited dissociative side effects in patients with TRD after a single intravenous dose of another formulation of R-ketamine.[6]

“We see great promise in PCN-101 as a potentially rapid-acting anti-depressant with a more favorable safety and tolerability profile than S-ketamine, which could enable at-home use,” said Florian Brand, CEO and Co-Founder of atai Life Sciences. “With today’s IND clearance, we are excited to continue assessing the therapeutic potential of PCN-101 in the U.S., where, like elsewhere in the world, many patients struggle with treatment-resistant depression and desperately need innovative therapeutic options.”

“TRD represents a large percentage of people with severe, difficult to treat depression who have failed to sufficiently respond to at least two different antidepressant treatments,” explained Terence Kelly, PhD, CEO of Perception Neuroscience, the atai Life Sciences platform company conducting the trials. “We believe that PCN-101 has the potential to offer a differentiated therapeutic effect, in terms of both efficacy and ease of administration, for clinicians and patients, as a potentially rapid-acting antidepressant. We look forward to progressing its clinical development.”

An estimated 100 million people live with TRD globally, representing a third of people with depression, who are undertreated or unresponsive to available treatment options.[7,8] In addition to its impact on patients, families, and caregivers, TRD severely impacts healthcare systems and payers. Direct medical costs for TRD patients are estimated to be two times higher than for non-TRD major depressive disorder (MDD) patients, with an average of twice the number of inpatient visits and hospital stays that are over one-third longer.[9,10]

This clinical DDI trial will advance alongside an existing Phase 2a proof-of-concept trial in TRD, recently initiated in Europe.[11] Additionally, atai anticipates running a bioavailability study in 2022, which is designed to bridge the IV formulation to a subcutaneous formulation of PCN-101, supporting the potential for self-administration.

About the clinical DDI study
The clinical study is an open-label, 2-cohort, fixed-sequence, drug-drug interaction study to evaluate the effects of CYP450 inhibition on the pharmacokinetics of PCN-101 in healthy adult subjects. atai will use the results of this study in conjunction with clinical pharmacokinetic data to advance the development of PCN-101 in TRD.

About PCN-101
Perception Neuroscience is developing PCN-101 (R-ketamine) for the treatment of TRD. PCN-101 is a single isomer of ketamine and belongs to a new generation of glutamate receptor modulators with the potential for rapid acting antidepressant (RAAD) activity and anti-suicidal effects. Pharmacologically, PCN-101 is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist. Nonclinical depression model studies in rodents suggest that R-ketamine could possess more durable effects and favorable safety and tolerability profile. Further supporting the potential of R-ketamine, an open-label clinical study has demonstrated rapid, durable response and limited dissociative side effects in TRD patients after a single intravenous dose.

About Perception Neuroscience, Inc
Perception Neuroscience is a New York City-based biopharmaceutical company committed to developing therapies for neuropsychiatric diseases. Perception's mission is to provide substantially more effective treatment solutions to serious psychiatric disorders. The company is a majority-owned subsidiary of atai Life Sciences.

About atai Life Sciences
atai is a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders. atai was founded in 2018 as a response to the significant unmet need and lack of innovation in the mental health treatment landscape. atai is dedicated to acquiring, incubating and

efficiently developing innovative therapeutics to treat depression, anxiety, addiction, and other mental health disorders.

atai's business model combines funding, technology, scientific and regulatory expertise with a focus on psychedelic therapy and other drugs with differentiated safety profiles and therapeutic potential. By pooling resources and best practices, atai aims to responsibly accelerate the development of new medicines across its companies, seeking to effectively treat and ultimately heal mental health disorders.

atai's vision is to heal mental health disorders so that everyone, everywhere can live a more fulfilled life. atai has offices in New York, London, and Berlin. For more information, please visit www.atai.life.

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Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “initiate,” “could,” “would,” “project,” “plan,” “potentially,” “preliminary,” “likely,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements include express or implied statements relating to, among other things: statements regarding the trials by Perception and future activities thereunder, the potential of PCN-101 (R-ketamine), the success, cost and timing of development of our product candidates, including the progress of preclinical and clinical trials and related milestones; our business strategy and plans; potential acquisitions; and the plans and objectives of management for future operations and capital expenditures. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond our control and which could cause actual results, levels of activity, performance or achievements to differ materially from those expressed or implied by these forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including without limitation: we are a clinical-stage biopharmaceutical company and have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future; we will require substantial additional funding to achieve our business goals, and if we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate our product development efforts; our limited operating history may make it difficult to evaluate the success of our business and to assess our future viability; we have never generated revenue and may never be profitable; our product candidates contain controlled substances, the use of which may generate public controversy; clinical and preclinical development is uncertain, and our preclinical programs may experience delays or may never advance to clinical trials; we rely on third parties to assist in conducting our clinical trials and some aspects of our research and preclinical testing, and those clinical trials, including progress and related milestones, may be impacted by several factors including the failure by such third parties to meet deadlines for the completion of such trials, research, or testing, changes to trial sites and other circumstances; we currently rely on qualified therapists working at third-party clinical trial sites to administer certain of our product candidates in our clinical trials and we expect this to continue upon approval, if any, of our current or future product candidates; if third-party sites fail to recruit and retain a sufficient number of therapists or effectively manage their therapists, our business, financial condition and results of operations would be materially harmed; we cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized; 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; we face significant competition in an environment of rapid technological and scientific change; third parties may claim that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent or delay our development and commercialization efforts; a change in our effective place of management may increase our aggregate tax burden; we identified

material weaknesses in connection with our internal control over financial reporting; and a pandemic, epidemic, or outbreak of an infectious disease, such as the COVID-19 pandemic, may materially and adversely affect our business, including our preclinical studies, clinical trials, third parties on whom we rely, our supply chain, our ability to raise capital, our ability to conduct regular business and our financial results. Other risk factors include the important factors described in the section titled “Risk Factors” in our final prospectus, dated June 17, 2021, filed with the Securities and Exchange Commission (“SEC”) pursuant to Rule 424(b) under the Securities Act, and in our other filings with the SEC, that may cause our actual results, performance or achievements to differ materially and adversely from those expressed or implied by the forward-looking statements.

Any forward-looking statements made herein speak only as of the date of this press release, and you should not rely on forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, performance, or achievements reflected in the forward-looking statements will be achieved or will occur. 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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