Azitra, Inc. Announces Positive Preclinical Data of ATR-12 and Clinical Design in Netherton Syndrome Presented at the ASGCT Annual Meeting

May 10, 2024 12:00 PM EDT

- ATR-12 has nanomolar inhibition of key protease *in vitro* that drives Netherton syndrome
- Topical application of ATR-12 to *ex vivo* human skin results in superior LEKTI delivery compared to topical LEKTI application
- ATR-12 reduces IL-36g, a pro-inflammatory cytokine that drives Netherton syndrome
- Safe and well tolerated in minipigs

BRANFORD, Conn.--(BUSINESS WIRE)--May 10, 2024-- Azitra, Inc. (NYSE American: AZTR), a clinical-stage biopharmaceutical company focused on developing innovative therapies for precision dermatology, today announced preclinical data from the Company's platform and pipeline. The data are being presented on Friday, May 10, 2024, in two oral sessions entitled "Engineered *Staphylococcus Epidermidis* as a Protein Delivery System for Treating Skin Diseases" and " *Staphylococcus epidermidis* Strain Expressing LEKTI-D6 (ATR12-351) for Netherton Syndrome" at the American Society of Gene and Cell Therapy (ASGCT) 2024 Annual Meeting in Baltimore, MD.

The data in the two oral presentations today showcase the preclinical development of ATR-12 and the clinical study design of a Phase 1b study in Netherton syndrome patients. *In vitro* data show that LEKTI (lympho-epithelial Kazal-type-related inhibitor) protein secreted by ATR-12 has nanomolar inhibition of a key protease that drives Netherton syndrome, kallikrein (KLK) 5 (IC_{50}=26 nM). Additionally, in human *ex vivo* Netherton syndrome models, ATR-12 supernatant reduces protease activity nearly 7-fold to levels comparable to healthy skin. Furthermore, in *ex vivo* human skin models, ATR-12 led to a higher amount of LEKTI delivery to the skin compared to topically applied LEKTI alone (6.1 $\mu g/cm^2$ vs. 2.3 $\mu g/cm^2$, p=0.008) after 24 hours and resulted in deeper biodistribution of LEKTI. Application of ATR-12 in human skin cell culture reduced IL-36γ by 92% compared to skin extracts induced to overexpress IL-36γ. Topical application of ATR-12 to *in vitro* human skin treated with erlotinib reduced IL-36γ by 69%.

In studies conducted in minipigs with abraded skin, topical application of ATR-12 resulted in 11.9 ng/cm^2 of LEKTI on the surface of the skin vs. 2.6 ng/cm^2 in the vehicle group at day 14. ATR-12 application was safe and well-tolerated in GLP toxicology studies with minipigs.

The oral presentation entitled "*Staphylococcus epidermidis* Strain Expressing LEKTI-D6 (ATR-12) for Netherton Syndrome" also provides the study design for an active clinical trial of ATR-12 in Netherton syndrome patients. The Phase 1b study (NCT06137157) is a multicenter, randomized, double-blind, vehicle-controlled study in adults (n=12) with Netherton syndrome. Patients will be treated twice daily with 10^9 CFU / g ATR-12 for 14 days. The primary objective is to assess the safety and tolerability of topical application of ATR-12, and the secondary objectives are to evaluate efficacy signals (e.g., investigator and patient global assessments) and to evaluate the skin pharmacokinetics of LEKTI. Exploratory objectives include the evaluation of pharmacodynamic parameters, including anti-LEKTI response, cytokine responses, biomarkers such as KLK5, KLK7, IL-36γ, trypsin-like activity, and chymotrypsin-like activity.

"We are thrilled to announce full preclinical data around ATR-12 as well as our clinical plan in Netherton syndrome that demonstrate proof-of-concept data supporting the use of genetically engineered skin commensals to deliver proteins to the skin," said Travis Whitfill, Azitra's co-founder and COO. "These data show the robust preclinical activity of ATR-12 in Netherton syndrome models and further supports the rationale behind our Phase 1b clinical trial in Netherton syndrome patients."

The presentations are now available on Azitra's website at https://ir.azitrainc.com/news-events/presentations.

About ATR-12

ATR-12 (also known as ATR12-351) is an engineered strain of *S. epidermidis* that expresses a fragment of human lympho-epithelial Kazal-type-related inhibitor (LEKTI) protein, which is missing in patients with Netherton syndrome, a chronic and sometimes fatal disease of the skin estimated to affect approximately one to nine in every 100,000. ATR-12 has been engineered to deliver missing LEKTI protein when applied topically to Netherton syndrome patients. Azitra has an open IND for a Phase 1b clinical trial in adult patients (NCT06137157). Azitra has secured clinical sites and identified Netherton syndrome patients for enrollment in its 12-patient, Phase 1b clinical trial, which will assess safety, tolerability, and efficacy endpoints. Azitra expects to announce initial safety data before year end.

About Azitra, Inc.

Azitra, Inc. is an early-stage clinical biopharmaceutical company focused on developing innovative therapies for precision dermatology using engineered proteins and topical live biotherapeutic products. The Company has built a proprietary platform that includes a microbial library comprised of approximately 1,500 unique bacterial strains that can be screened for unique therapeutic characteristics. The platform is augmented by artificial intelligence and machine learning technology that analyzes, predicts, and helps screen the Company's library of strains for drug like molecules. The Company's initial focus is on the development of genetically engineered strains of Staphylococcus epidermidis, or *S. epidermidis*, which the Company considers to be an optimal therapeutic candidate species for engineering of dermatologic therapies. For more information, please visit https://azitrainc.com/.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding the expected timing of the presentation of data from the Phase 1b study of ATR-12, the filing of an IND application, and the presentation of data from our Phase 1b for ATR-04, the IND filing for ATR-01, the timing of having a signed license agreement with Bayer, and statements about our clinical and pre-clinical programs, and corporate and clinical/pre-clinical strategies.

Any forward-looking statements in this press release are based on current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to that we may fail to successfully complete our Phase 1b trial for ATR-12 and pre-clinical studies of other product candidates and obtain required approval before commercialization; our product candidates may not be effective; there may be delays in regulatory approval or changes in regulatory framework that are out of our control; our estimation of addressable markets of our product candidates may be inaccurate; we may fail to timely raise additional required funding; more efficient competitors or more effective competing treatment may emerge; we may be involved in disputes surrounding the use of our intellectual property crucial to our success; we may not be able to attract and retain key employees and qualified personnel; earlier study results may not be predictive of later stage study outcomes; and we are dependent on third-parties for some or all aspects of our product manufacturing, research and preclinical and clinical testing. Additional risks concerning Azitra's programs and operations are described in its annual report on Form 10-K filed with the SEC on March 15, 2024. Azitra explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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Norman Staskey
Chief Financial Officer
staskey@azitrainc.com

Hayden IR
James Carbonara
(646) 755-7412
james@haydenir.com

Source: Azitra, Inc.