Attralus Announces Publication of Two Studies Evaluating Iodine (^{124}I) Evuzamitide (AT-01) using PET/CT in the Journal of American College of Cardiology (JACC CV Imaging)

- *^{124}I-evuzamitide shown to be highly accurate for detection of cardiac amyloid across two independent investigator-initiated studies.*
- *^{124}I-evuzamitide detects multiple types of systemic amyloidosis.*
- *^{124}I-evuzamitide may be more sensitive than standard diagnostics, with cardiac uptake shown in ATTR patients who had negative ^{99m}Tc-PYP scans.*
- *Moderate-to-strong correlations were observed with ^{124}I-evuzamitide uptake and structural and functional cardiac imaging measures, health related quality of life (HRQoL), and cardiac biomarkers.*

SAN FRANCISCO, Calif. – November 07, 2023 – Attralus, Inc., a clinical stage biopharmaceutical company developing transformative medicines to improve the lives of patients with systemic amyloidosis, today announced the publication of results from two Attralus-funded investigator-initiated studies of ^{124}I-evuzamitide, the company's investigational pan-amyloid radiotracer under development for the diagnosis and management of systemic amyloidosis. The manuscripts from Brigham and Women's Hospital (BWH) and from the University of Tennessee Graduate School of Medicine were published in the *Journal of American College of Cardiology – Cardiovascular Imaging* (JACC CV Imaging). The manuscripts, entitled "Cardiac Amyloid Quantification Using ^{124}I-Evuzamitide (^{124}I-P5+14) Versus ^{18}F-Florbetapir" and "Cardiac Amyloid Detection by PET/CT Imaging of Iodine (124I)

Evuzamitide (124I-p5+14): A Phase 1/2 Study," have been published online. These two manuscripts were also accompanied by an editorial entitled "Shining a Radiant Light on Cardiac Amyloidosis with Novel ^{124}I-Evuzamitide PET Imaging." All three articles can be found online here.

The key data reported in the publications show PET/CT imaging of patients with diverse types of systemic amyloidosis with visually appreciable uptake in the heart with high sensitivity and other organs suspected of amyloid involvement and highlighted that ^{124}I-evuzamitide imaging may detect cardiac amyloid prior to clinical manifestation.

Furthermore, ^{124}I-evuzamitide was shown to accurately discriminate amyloid cardiomyopathy (CMP) from controls. In patients with ATTRwt-CMP, performance may be better with ^{124}I-evuzamitide, as evidenced by significantly higher uptake than ^{18}F-florbetapir, and higher uptake than in AL patients aligning with literature that ATTR patients have a higher cardiac amyloid load. Moderate-to-strong correlations between ^{124}I-evuzamitide uptake and cardiac structural and functional measures utilizing echocardiography and cardiac magnetic resonance imaging, health related quality of life (HRQoL) metrics, and cardiac biomarkers were observed. The results also support the potential of ^{124}I-evuzamitide as a pan-amyloid imaging agent, with positive cardiac uptake also seen in AApoAIV, AApoA1 and ALys amyloidosis patients. Infusion of ^{124}I-evuzamitide was generally safe and well tolerated in these studies.

These studies suggest that ^{124}I-evuzamitide is a promising novel radiotracer to detect and quantify cardiac amyloid in multiple types of amyloidosis. Furthermore, the authors from BWH study stated that the ability of ^{124}I-evuzamitide to specifically bind to amyloid deposits is promising for the ongoing Phase I trial investigating a monoclonal antibody fusion protein incorporating a similar amyloid-binding peptide, which targets amyloid deposits to trigger their removal.

"Cardiac amyloidosis is an underdiagnosed condition. Despite recent improvements, diagnosis continues to be a challenge. There is an unmet need for more sensitive and specific diagnostics" said Professor Sharmila Dorbala MD, MPH, Harvard Medical School, Cardiovascular Medicine, and lead author of the BWH study. "In our study, I-124 evuzamitide perfectly discriminated between healthy subjects and both AL and ATTR cardiac amyloidosis patients. In ATTR patients, myocardial uptake was significantly higher with I-124 evuzamitide than with F18-florbetapir, suggesting that diagnostic performance may be better with I-124 evuzamitide. Although not evaluated in this study, direct amyloid quantification with I-124 evuzamitide may be useful for diagnosis of early disease and for monitoring disease progression or response to treatment. We were particularly

encouraged by the moderate to strong correlations between amyloid quantitation by I-124 evuzamitide and health-related quality of life metrics, cardiac biomarkers, and standard imaging measures of structure and function."

"Detection and quantification of amyloid burden in the heart is an unmet clinical need for patients with diverse types of systemic amyloidosis," said Jonathan Wall, Ph.D., Distinguished Professor, University of Tennessee Graduate School of Medicine. "The iodine-124 evuzamitide radiotracer has the potential to be an invaluable tool to both detect early cardiac and extracardiac deposits and to quantify amyloid burden."

Summary of Published Results

BWH study

This pilot study enrolled 26 patients with systemic amyloidosis (12 AL, 12 ATTR and 2 other types) and 12 healthy volunteers (HVs). Eight additional HVs were included in the publication from a ^{18}F-florbetapir study to compare the accuracy of ^{18}F- florbetapir to ^{124}I-evuzamitide. The BWH study is the first to systematically evaluate myocardial uptake of ^{124}I-evuzamitide compared to standard imaging modalities, clinical metrics, and HRQoL parameters in a cohort of participants with amyloid CMP, and the first to compare it to ^{18}F- florbetapir. The study evaluated the quantitative myocardial uptake of ^{124}I-evuzamitide and measured correlations between ^{124}I-evuzamitide and clinical markers of amyloid CMP. All patients received an IV infusion of 1 mCi of ^{124}I-evuzamitide and images were acquired at 5 hours post injection.

- Quantitative uptake of ^{124}I-evuzamitide perfectly discriminated all cases of known AL-CMP and ATTRwt-CMP from controls, using measures of left ventricular % injected dose (LV %ID), cardiac amyloid activity (CAA), and target to background ratio (TBR).
- When comparing radiotracers, ^{124}I-evuzamitide consistently showed higher myocardial uptake in patients with ATTRwt amyloidosis, suggesting that it may perform better in these patients. The performance was similar to ^{18}F- florbetapir in AL Amyloidosis.
- Furthermore, among AL and ATTRwt participants, ^{124}I-evuzamitide LV %ID was moderately to strongly correlated with indirect metrics of amyloid burden, both structural and functional (interventricular septum thickness, LV mass index, MCF, GLS, ECV), assessed using standard echocardiographic and MRI techniques, suggesting valid amyloid burden quantitation.

- Cardiac uptake of ^{124}I-evuzamitide strongly correlated with cardiac-related serum biomarkers (NT-proBNP and troponin), and moderately to strongly correlated with clinical and HRQoL measures, suggesting meaningfulness to patients.
- The results also include a case in which an ATTRwt patient showed positive cardiac uptake of ^{124}I-evuzamitide, a negative ^{99m}Tc-PYP scan, with an amyloid positive cardiac biopsy, suggesting ^{124}I-evuzamitide may be more sensitive than *^{99m}Tc-PYP.*
- No cardiac uptake was observed in HVs.

The results suggest that ^{124}I-evuzamitide can accurately detect and quantify cardiac amyloid burden. With further validation, quantitative ^{124}I-evuzamitide uptake may be particularly useful to diagnose early disease or to monitor disease progression or response to therapy in subjects with cardiac amyloidosis.

UT study

The first in human Phase 1/2 trial evaluated the ability of ^{124}I-evuzamitide to detect amyloid deposits by PET/CT imaging in patients with diverse forms of systemic amyloidosis. The trial enrolled 50 systemic amyloidosis pts (23 AL, 20 ATTR and 7 other types) and 5 HVs. All patients received an IV infusion of <2 mg of ^{124}I-evuzamitide (≤2 mCi of I-124) and images were acquired at ~5 hours post injection. Efficacy endpoints included patient- and organ-based sensitivity of ^{124}I-evuzamitide uptake in the heart, liver, spleen, and kidney.

- Cardiac uptake of the radiotracer was observed in 100% of patients with ATTR in whom clinical evidence supported a diagnosis of amyloid CMP.
- Positive cardiac PET/CT imaging was observed in six patients with a diagnosis of ATTR amyloidosis but no clinical evidence of cardiac involvement, with negative ^{99m}Tc-PYP imaging and normal serum NTproBNP levels. At least one of these subjects had a confirmatory cardiac biopsy confirming ATTR amyloidosis in the heart.
- Of the major abdominothoracic organs, the sensitivity (positive percent agreement) between clinical findings and ^{124}I-evuzamitide imaging was strongest for the heart (96.2%; 95% CI: 80.4-99.9; *n*=25/26). PET/CT imaging of ^{124}I-evuzamitide in patients with ATTR and AL amyloidosis exhibited diverse anatomic uptake involving e.g., the lung, liver, kidney, pancreas, spheroid joints, spine, and abdominal fat, consistent with the systemic nature of these

diseases, and with previously published autopsy findings. These data suggest that ^{124}I-evuzamitide imaging can detect not only cardiac amyloidosis, but also extracardiac disease.

- No cardiac uptake was observed in HVs.

The data from this first-in-human study supports the overall safety and efficacy of ^{124}I-evuzamitide for detecting cardiac amyloidosis, as well as systemic amyloid deposits.

About Systemic Amyloidosis

Systemic amyloidosis encompasses a diverse group of rare diseases that occur due to accumulation of toxic amyloid deposits in tissues and organs, a consequence of aberrant protein misfolding events. These diseases are progressive, debilitating and often fatal. Systemic amyloidosis is significantly underdiagnosed due to low awareness, lack of specific symptoms, and no current disease-specific diagnostics. The two most common forms of systemic amyloidosis are immunoglobulin light-chain-associated (AL) amyloidosis and transthyretin-associated amyloidosis (ATTR). There is a significant unmet need for new therapies and diagnostics in systemic amyloidosis.

About I-124-EVUZAMITIDE Pan-Amyloid Diagnostic (Also known as AT-01)

I-124-EVUZAMITIDE (iodine-124 Evuzamitide) utilizes the company's pan-amyloid binding peptide as an amyloid-specific imaging agent to image all types of systemic amyloidosis by PET/CT imaging. In initial clinical trials, I-124-EVUZAMITIDE has been shown to detect multiple types of amyloid deposits, including AL and ATTR, in major organs such as the heart, kidney, liver and spleen. Attralus obtained exclusive rights to commercialize I-124-EVUZAMITIDE under a commercial license agreement with the University of Tennessee Research Foundation. The same PAR-peptide technology is utilized in AT-02 and AT-04, two of the company's therapeutic candidates.

About Attralus

Attralus is a clinical stage biopharmaceutical company focused on creating transformative medicines to improve the lives of patients with systemic amyloidosis. The company's proprietary pan-amyloid removal (PAR) therapeutics are designed to directly bind to and remove toxic amyloid in organs and tissues. By targeting the universal disease-causing pathology in systemic amyloidosis diseases, PAR therapeutics have the potential to treat and reverse disease in patients with all types and stages of systemic amyloidosis. Attralus was founded by scientific experts in the field of amyloidosis and the company is headquartered in San Francisco.

Forward-Looking Statements

This press release contains forward-looking statements, including statements related to the efficacy, continued development, and potential of the Company's product candidates. Words such as "novel," "developing," "first and only," "potential," "shown" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Attralus' current expectations. Forward-looking statements involve risks and uncertainties. Attralus' actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties. Attralus expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Attralus' expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

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