Arterez™
*Targeting upstream disease etiology*

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**Technology Platform: (FDA Reviewed)**

Anti-Thrombotic Oral Therapies
- Embotricin™
  *MOA: endothelial glycocalyx repair, inflammation and oxidation*

Multiplex Diagnostic Tools
- GlycoCardia™
  *4-marker kit to monitor drug efficacy*
- Glycalyx Detritus Fingerprint™
  *7-marker kit for disease identification, staging & characterization*

**Intellectual Properties:**

(*Issued*) Biomarkers of Vascular Disease
(*Issued*) Methods and Compositions for Reversing Disruption of the Glycocalyx, Inflammation and Oxidative Damage
(*Pending*) Drug Treatment & Biomarker Panel Targeted to Diseases Due to Multifactorial Ontology of Glycocalyx Disruption
(*Draft*) Animal Model for CVD & Inflammation
PCT and additional filings in process
Multiple trademarks awarded and in process

**Clinical Targets:**

Embotricin™ FDA IND indications:
- *Pulmonary Hypertension*
- *Dialysis Fistula (IND optional)*

Embotricin™ Proof of Principle/non-US:
- *Heart Failure*
- *Coronary Artery Disease*

GlycoCardia™ multiplex
- *Surrogate markers to measure drug effect*

**Pre-clinical Providers:**

DSK – GLP *compound manufacturing*
Wayne State Bio – *ELISA studies*
Henry Ford Hospital – *translational studies*
Camargo Research – *CRO selection, oversight*
Camargo Regulatory – FDA, *regulatory*
Theraquila – *in vitro, in vivo toxicology*
Utah State – *pollutant & optimization*
Clinical Network Svcs – *GAP analysis/AUS*

**Clinical Providers:**

Cambrex – *GMP manufacturing & formulation*
Transhit-Bio – *clinical bio-samples sourcing*
Arbor Assays – *7-disease ELISA pilots*
M. Perera, PhD – Analysis & *Algorithms*
Dr. Bonnie Weiner – *clinical strategy & PI*
TBD – *clinical investigator (US and AUS)*

**Legal and Advisory:**

Weaver Austin Villeneuve & Sampson LLP
*Intellectual Properties*
Bodman PLC
*Corporate filings, offering documentation*
Varnum LLP
*Trademarks, Publishing*
Garrett & Bachand PC
*General counsel & advisory*
*Croskey Lanni PC*
*Corporate Accounting*
ABA Consulting
*Corporate Advisory (AUS)*

Cardiovascular Disease (CVD) is the world's leading chronic disease killer impacting more than one-third of the world's population. Among the top 150 developing nations worldwide, CVD is the largest health risk and cost. In the 1940's, the discovery of penicillin spawned the antibiotic industry and the treatment paradigm of one antibiotic to one microbial infection which effectively eliminated the targeted microbe and cured the corresponding disease. This one-drug-one-disease paradigm was carried over to the current treatment of other diseases, however mono-therapies cannot address the multifactorial etiology of chronic diseases.

Arterez. Inc. is a late-stage pre-clinical company with FDA pre-IND completed for our lead therapeutic drug, Embotricin™. Our platform involves proprietary combo therapies and multi-marker diagnostics to address the multifactorial nature of chronic disease which starts with the disruption of the cell's protective shield, the glycocalyx, triggered by a number of environmental and extraneous factors leading to oxidative damage and inflammatory response we've identified collectively as the upstream causes. If this vicious cycle and sequela of damage continues, it manifests into various downstream symptoms which are what are being treated with current monotherapies. Treating symptoms of disease downstream is precisely why symptom-targeted drugs cannot cure or prevent disease and are at best palliative.

Initially, we chose cardiovascular disease (CVD) for proof-of-principle of our combo paradigm. Embotricin™ (a triple component oral drug) is our lead therapeutic, which proved curative and preventive of arterial plaque in preclinical studies. The effective dose in mice is 3mg/kg with no-observed-adverse-effect-level (NOAEL) at 1,000 mg/kg further confirmed by rat in vivo and histopathology indicating Embotricin™ to be non-toxic with a wide therapeutic window. Preventive and curative treatment effect was confirmed by 4 biomarkers identified from shed glycocalyx detritus clinically correlated to arterial plaques we have since established and patented as a surrogate marker kit to monitor treatment effect, GlycoCardia™ in addition to histopathology and magnetic resonance imaging (MRI) to confirm results.

Glycocalyx disruption generates debris (detritus), which is quantitated by antibody levels; the levels of debris shed to the blood stream is unique to every disease, which is the foundation of GlycoCardia™ and Arterez' Glycalyx Detritus Fingerprint™ (GDF) technology, another proprietary core technology involving the attachment of 7 antibody-analyte complex to color-coded microbeads with fluorescent reporter dye labels; 10X more sensitive and faster (3-hr) than ELISA (60-hr turnaround). Current diagnostics involve one biomarker per disease, which is neither dependable nor accurate. The multi-component GDF offers pattern recognition to provide an accurate fingerprinting system for disease.

## TECHNOLOGY BRIEF

Dr. Tunac developed and synthesized 9 active compounds leading to Arterez' first 3-drug combo Embotricin™ as well as a 4-panel companion diagnostic tool to monitor endothelial glycocalyx health, GlycoCardia™, and finally the Glycocalyx Detritus Fingerprint™, a 7-panel universal diagnostic tool for chronic disease. These are Arterez' first drug and diagnostics platform technologies in our development pipeline.

- Embotricin™ proved to prevent plaque formation and /or restored the integrity of the endothelial glycocalyx as evidenced by the reduction in glycocalyx detritus shed in the bloodstream measured by individual biomarkers that make up the diagnostic panel, GlycoCardia™.
- The effective dose in mice is 3mg/kg with no-observed-adverse-effect-level (NOAEL) up to 1,000 mg/kg in mice and 800mg/kg in rats confirmed by histopathology indicating Embotricin™ is non-toxic.
- GlycoCardia™ utilizes 4 detritus biomarkers including heparan sulfate (HS), Hyaluronan synthase-1 (HAS-), syndecan-1 (SDC-1), and plasminogen activator inhibitor-1 (PAI-1). It is being developed as a companion diagnostic for plaque formation/regression to monitor Embotricin™ efficacy and will be presented as a surrogate end-point to the FDA.
- The Glycalyx Detritus Fingerprint™ (GDF) consists of the 4 GlycoCardia™ components plus 3 additional biomarkers, including Gamma (γ') fibrinogen (FGG), Growth differentiation factor 15 (GDF-15) and Pregnancy associated plasma protein (PAPP-A). The GDF 7-marker panel is being developed as a universal diagnostic tool for chronic diseases, equivalent to the DNA Fingerprint in forensics.
- Licensing and/or co-development opportunities will be pursued for the diagnostic platform in 2022.
- First in-human 'proof of principle' POC studies against hypertension, heart failure and coronary artery disease are expected to begin 2024 and will run concurrently.

## CAPITAL RAISE

Arterez is seeking $12.5 M to reach FDA IND, comprised of a $2.5 M Bridge open to accredited investors leading to a $10 million Series A round. IPO option available at IND milestone (18-24 mths) to fund 3 concurrent first in-human efficacy studies against heart failure, coronary artery disease and hypertension, and to bring forward pipeline drugs in development.

Exit strategy involves diagnostic licensing (12-18 mos.) and licensing and/or acquisition of Embotricin against one or more indications pre-FDA NDA (32-36 mos.) and public offering to enable further pipeline development.

## About Dr. Joe Tunac, Inventor, Founder, President & Chairman

Dr. Joe Tunac is a medical scientist specializing in the discovery and development of drugs. He studies the biochemistry and physiology of the human body and designs drugs to target dysfunctional mechanisms with great success. He obtained his undergraduate degree from the University of the Philippines, then graduate studies at South Dakota State, Penn State Universtiy and a doctorate degree from Rutgers, where he studied at the Waksman Institute, the world center for antibiotics.

Merck hired Dr. Tunac as a senior scientist where he was instrumental in the discovery and development of multi-billion dollar drugs, moved to Parke-Davis where he continued drug development and commercialization, then left for independent entrepreneurial research and development, commercializing drugs and medical products on a global scale. He has more than 40 years of experience, over 30 patents and patents pending and more than 35 scientific publications.

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