Caradon
THERAPEUTICS

# Pioneering novel long-acting peptides for cardiometabolic diseases in humans and animals

# Caradon's innovative approach and opportunity in human and animal health

| | |
|---|---|
| Novel Approach Based on Clinical Validation | • We develop long-acting CRF2 peptide agonists by engineering native peptides with established preclinical and clinical safety<br>• Our lead mechanism enhances cardiac output without increasing myocardial oxygen demand—a unique, disease-modifying inotropic effect<br>**>> Our approach builds on clinically validated biology, optimized for chronic use** |
| Lead Programs (CARE110/210) | • CARE110 (human health) and CARE210 (animal health) are long-acting CRF2 agonists designed for chronic forms of heart failure<br>• Extended half-life enables outpatient treatment and unlocks new indications in cardiovascular and metabolic diseases<br>**>> Our pipeline targets large, underserved markets in human and veterinary medicine** |
| CRF2/Urocortin Domain Expertise | • Our team led the initial development of CRF1 and CRF2 agonists at J&J, developing unparalleled clinical and translational experience with this mechanism<br>• Foundational knowledge of the native CRF2 target underpins our lead CARE110/210 programs and our broader pipeline<br>**>> Caradon's CRF1 and CRF2 agonist domain expertise is unmatched** |
| Proven Team and Platform | • Caradon was founded by the same team behind Antlia Bioscience (NIH- and VC-backed), leveraging a validated strategy and enabling PASylation® platform<br>• We apply this technology to clinically validated peptides, transforming them into first-in-class therapeutics for chronic use<br>**>> Proven team, platform, and path to value across human and animal health** |

Caradon THERAPEUTICS

# Proven management team with deep knowledge developing peptide agonists

## BRIAN L. JOHNSON J.D. (Founder)

**Chief Executive Officer**

Brian is a serial company founder, executive, and board director with 25+ years of experience across drug development, operations, risk management and regulatory compliance. A lawyer by training but a drug developer by choice. Founder and Board member @Antlia Bioscience, Inc.

## NIGEL SHANKLEY PH.D. (Founder)

**Chief Scientific Officer**

Nigel is a founder and pharmacologist with 35+ years of experience in research and development. Former Discovery Head of Cardiovascular and Metabolic group for Janssen R&D, and former Global Head of External Innovation for Janssen's cardiovascular and metabolic diseases therapeutic area. While at Janssen, Nigel oversaw the development of the acute and long acting stresscopin for heart failure.

## TIMOTHY SIMON (Advisor)

**Strategy & Business Advisor**

Tim is a biotech executive with extensive experience bringing drugs to market and has held executive leadership positions at multiple Pharma companies with 3B+ P&L responsibility. He also has a strong M&A background and has executed many out-licenses and acquisitions. Tim currently heads the M&A department at a mid-cap biotechnology company.

## DAWN BELL, PHARMD (Founder/Advisor)

**CEO @Antlia Bioscience, Inc.**

Dawn is a founder, operator, and board director with diverse experience across drug development and commercialization spanning BD&L, portfolio strategy, R&D, medical affairs, and market access in both private and public companies (NYSE: NVS; NASDAQ: MDCO).

## JACK SPITZBERG, M.D., FACP, FACC (Advisor)

**Clinical Cardiologist and Clinical Advisor**

Dr. Spitzberg is a diagnostic and invasive cardiologist, specializing in hypertension, coronary artery disease, and heart failure. He is board-certified in cardiology and internal medicine and currently practicing with Cardiology and Interventional Vascular Associates of Dallas, Texas. Advisor @Antlia Bioscience, Inc.

## GILL SAWHNEY (Advisor)

**CFO & Corporate Strategy Advisor**

Gill is an executive with 25+ years in Investment banking and corporate strategy consulting experience with life science companies from startup through commercial launch. He has closed over 115 financing and M&A/advisory transactions, including leading over 30 IPOs for companies including Arena, Cubist, MiniMed and Axsome.

Advisor @Antlia Bioscience, Inc.

Caradon THERAPEUTICS

# Proven management team with deep knowledge developing peptide agonists (2/2)

## HANI "TONY" SABBAH, PH.D (Development Advisor)

**Section Head, Cardiovascular Research**
**Henry Ford Health System**

Dr. Sabbah is a Professor of Medicine at Wayne State University and the Director of CV Research at the Henry Ford Health System. Dr. Sabbah's lab developed and runs the premier validated model of ischemic heart failure in canines. Dr. Sabbah is also an Advisor @Antlia Bioscience, Inc.

## CHRISTOPHER KROEGER, M.D., MBA (Advisor)

**Clinical and Business Advisor**

Dr. Kroeger has 20+ years of leading, building, and advising development-stage therapeutic companies. Previous CEO of Cardioxyl Pharma (sold to BMS for $2.1B) and current CEO of MapLight Therapeutics (recently closed a capital round in excess of $300M) to pursue various CNS diseases. Dr. Kroeger is also an Advisor @Antlia Bioscience, Inc.

## RONALD V .SWANSON, PH.D (Investor and Advisor)

**Science and Biology Advisor**

Dr. Swanson is the CSO at Tyra Bioscience and brings 26+ years of biotech and pharma experience. Prior to joining Tyra, Dr. Swanson was as Senior Director, Biologics at Johnson & Johnson, Inc. where he focused on engineering peptides and protein therapeutics. Dr. Swanson was a post-doc at Caltech, holds a B.A. in Biochemistry and Cell Biology from UCSD and a Ph.D. in Molecular Biology from the University of California, Berkeley.

## TERRY BARRETT, PH.D (Advisor and Investor)

**Pre-clinical and Clinical Advisor**

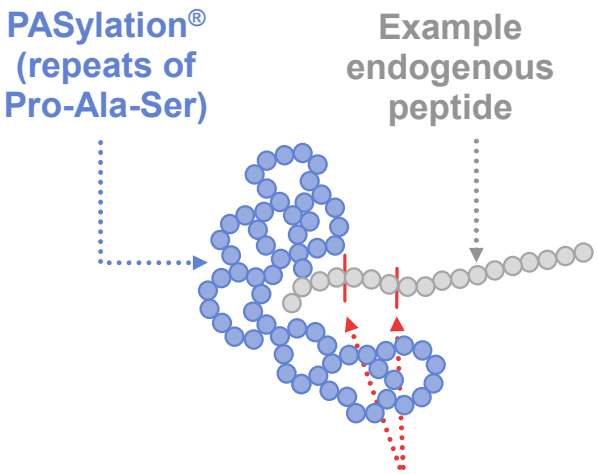
Dr. Barrett is a cardiovascular pharmacologist by training and an expert in translation from pre-clinical to clinical proof-of-concept studies in the cardiovascular, metabolic, renal and hematology therapeutics areas. Dr. Barrett is currently Director of Clinical Development at Ionis Pharmaceuticals and former drug discovery and early development leader at Janssen. Dr. Barrett is a founder @Eleven Therapeutics Corp.

Caradon THERAPEUTICS

# Caradon's unique technology: Our Long-Acting CRF2 Agonists harnesses the endogenous system while allowing for weekly subcutaneous dosing

## CARE110/210




**Peptide half life dramatically extended via PAS structure, while preserving function**

=

## Native CRF2 Agonist

- **Endogenous** peptide
- **Master regulator,** widely expressed and acts through the cardiovascular, renal, metabolic, and muscular systems
- **Validated mechanism**
  - **Clinically validated in heart failure** through phase II in humans
  - **Preclinical** validation in translational disease models of heart failure, pulmonary hypertension, sarcopenia and weight loss
- **Significant interest** in CRF2 agonists from strategic pharma and venture capital

+

## Proprietary Enabling Technology PASylation®

- Proprietary technology that extends half-life for **daily to 1x weekly dosing**
- **Technology Reviewed by FDA** and currently in multiple US clinical trials (Jazz and Akari)
- **Highly tunable** to each disease indication and market opportunity
- Multiple **composition of matter** patents and provisional patents
- **Scalable & low COGS** coupled with manufacturers that have PASylation® experience
- **Superior** to other half-life enabling technologies

Caradon THERAPEUTICS

# Our long-acting CRF2 has potential for significant advancement in heart failure (HF) and other cardiometabolic diseases, all of which present large commercial opportunities

| | | |
|---|---|---|
| **HEART FAILURE (Reduced or Preserved Ejection Fraction)** | **>$10B** Domestic US | • Our long-acting CRF2 agonist presents a promising and novel opportunity to treat all forms of chronic heart failure simultaneously improving the heart's contractility (inotropic effect) and enhance its relaxation (lusitropic effect) without increasing myocardial energy demands.<br>• Proof-of-concept studies in heart failure patients and in preclinical HF models, CRF2 agonists:<br>  • Improve cardiac function, renal function, and reduce pulmonary congestion without tachycardia or increase in O2 consumption<br>  • Preclinical study in dog ischemic heart failure model showed 1x month therapeutic exposure resulted in clear indication of reverse remodeling, reduction in fibrosis and inflammation. |
| **HEART FAILURE (Animal Health)** | **>$6B** Domestic US | • HF in animal health represents a significant early market opportunity. The efficacy and safety of the native peptide is already demonstrated in large canine ischemic heart failure model. We intend to run our compounds through the same efficacy model.<br>• There is notable interest from strategic animal health pharmaceutical companies, presenting a chance for initial revenue via a license of shelf-compound. |
| **ACUTE HEART FAILURE** | **>$1B** Domestic US | • Standard diuretics do not yield long-term improvements in cardiac function or long-term reductions rehospitalization rates. Our long-acting CRF2 agonist presents a promising opportunity to promote diuresis/natriuresis and improve cardiovascular and renal function. This indication allows for a smaller non-outcomes-based clinical trial and reduced dev. costs. |

Caradon THERAPEUTICS

# Expansion into other therapeutic areas: Our long-acting CRF2 agonist has potential to fundamentally change treatment in other large markets

| | | |
|---|---|---|
| **PULMONARY ARTERIAL HYPERTENSION (including other forms of PH)** | **>$7B** Domestic US | • PH is a feature of a variety of diseases and continues to harbor high morbidity mortality affecting 10% of individuals >65 years of age.<br>• Based on pre-clinical models, CRF2 agonist present a promising opportunity in PH<br>• CRF2 agonism has been shown effective in experimental models of PH by:<br>  • Reducing the left ventricular filling pressure<br>  • Improving right cardiac function and pulmonary arterial resistance<br>  • Improving the cardiac remodeling |
| **SARCOPENIA** | **>$10B** Domestic US | • Sarcopenia is characterized by age-related decline of muscle mass and muscle function, which impacts ~24% of people >65<br>• Based on pre-clinical models, CRF2 agonists present a promising opportunity to treat sarcopenia<br>• CRF2 agonism has been shown effective in experimental studies resulting in:<br>  • reduce skeletal muscle mass wasting, improve muscle strength, and enhance exercise capacity in multiple models of sarcopenia |
| **OBESITY** | **>$30B** Domestic US | •Based on evidence from pre-clinical models, our long-acting CRF2 agonist presents the potential for a novel drug that reduces fat mass, while preserving lean mass:<br>  • This presents a potential therapeutic option for managing obesity in a broader set of patients, particularly those with comorbid conditions<br>  • We intend to explore developing a novel combination therapy with our CARE110 compound and a GLP1, using PASylation as the linker |

Caradon THERAPEUTICS

## First therapeutic area of focus: Our long-acting CRF2 agonist represents a significant advancement in the treatment of heart failure

### Current HF Drugs

Existing drugs reduce the overall load on the heart BUT FAIL to address reductions in cardiac output and reserve

### Prior Attempts to Develop Inotropic Drugs

Historic focus was stimulating cAMP to increase cardiac output AT THE EXPENSE of increased cardiac energy demands

**Effective in the short-term but highly problematic in the long-term**

### Caradon Solution
Long-acting PASylated® CRF2 agonist

A novel acute acting lusitrope and long-acting inotrope that can restore cardiac function WITHOUT increasing overall energy demands or impacting heart rate or blood pressure

Strong potential for reverse remodeling (reduction in inflammation and fibrosis)

**There is a large unmet need for a heart failure drug that can restore cardiac function without increasing energy demands with potential reverse remodeling**

Caradon THERAPEUTICS

# Caradon has a versatile go-to-market strategy with early revenue and composition of matter IP

## Multiple Pipeline Development and Commercialization Possibilities via PAS Size Variation

- Each sized PASylated® compound is a unique and new chemical entity that can be tuned for route of administration, frequency of dosing, and targeted to specific disease
- Allows for separate INDs for each different sized PASylated® compound and corresponding indication allowing for targeted marketing and pricing strategies
- Ability to license specific-sized PASylated® compounds on an indication-by-indication basis (e.g., license PAS200 SCP for animal health, but continue to retain rights to all other PAS SCP compounds for human indications)
- Potential for combination products using PASylation® as a linker with other promising targets like GLP1 or BNP (e.g., CARE110-PAS-CAREXXX)

## Comprehensive Intellectual Property Strategy

- Strong intellectual property covering both the in-licensed PASylation® enabling technology and Caradon 110/210 development programs
- Provisional composition of matter patents for PASylated CRF2 agonist with a priority date of 2023
- Full PCT patent filed for PASylated CRF2 agonist 2025
- Caradon patents builds on existing in-licensed IP portfolio for the PASylation® platform

Caradon THERAPEUTICS

# Big Pharma and venture capital understand and have invested in the CRF2 agonist pathway

CORTERIA PHARMACEUTICALS

- Spun out of Sanofi 2023 and like Caradon is developing a CRF2 agonist
- Targets the same disease indications as Caradon (HF, Sarcopenia, RHF/PH, and Obesity)
- Received $70M in funding from Sanofi and tier 1 venture capital
- Utilizes undisclosed enabling technology to extend the half-life of their CRF2 agonist
- Focus is daily and up to 1x monthly dosing

## Limitations of Corteria Approach

- **Lacks the ability to tune their compounds' pharmacokinetics resulting in only two potential dosing options (1x daily or ~1x monthly)**
- **Increased chance of immunogenicity and anti-drug antibodies**
- **Increased manufacturing complexity and associated costs**

## Impact for Caradon

- ✓ Validates both the CRF2 pathway approach and the target indications
- ✓ Corteria doesn't have the benefit of the years of learnings developing a CRF2 agonist
- ✓ We focus on a different CRF2 agonist. Based on our prior experience with both agonists, our approach has superior efficacy and safety as compared to the agonist developed by Corteria
- ✓ PASylation® gives us the ability to strategically tune our compounds
- ✓ Target indications are exceptionally large markets that can support multiple drugs
- ✓ With our platform approach, we have early revenue opportunities in animal health and the ability to continue to develop distinct CTE compounds for human diseases

# The target native CRF2 agonist was previously validated in preclinical models of acute and chronic exposure in advanced Ischemia-induced HF in dogs

- Program was led by Caradon Co-Founder/CSO Nigel Shankley, Ph.D., and advisor/investor Ron Swanson Ph.D.
- Evaluated CRF2 agonist in both healthy dogs and a chronic model of advanced ischemia-induced heart failure. The Results of the chronic dog study is not public.
- The acute and the chronic studies both point to the novel inotropic effects of acute and long-term exposure to the CRF2 agonist without the increase in MV02
- See abstract on results of acute study Gengo et al, Circulation 126, Abstract 15421 (SCP-AHA 2012)

**Abstract 15421: Acute Intravenous Infusion of Human Stresscopin (JNJ-39588146) Improves Left Ventricular Systolic Performance in Dogs with Advanced Heart Failure**

Peter J Gengo[1]; Mengjun Wang[2]; Kefei Zhang[2]; Itamar Ilsar[2]; Ramesh C Gupta[2]; Sharad Rastogi[2]; David Uhlinger[1]; Katherine Figueroa[1]; Nigel P Shankley[1]; Hani N Sabbah[2]

## Administration of therapeutic doses of native CRF2 agonist produced

- Increased left ventricular (LV) contractile performance
- Increased LV ejection fraction (LVEF)
- Increased cardiac output (CO)
- Increased stroke volume (SV)
- No increase in myocardial oxygen consumption (MV02)
- Reverse remodeling seen after ~30 days of continues exposure

## Additional observations

- The increase in CO were not associated with changes in heart rate or blood pressure
- Only at high doses above the therapeutic range does the CRF2 agonist behave as vasodilator with reflex tachycardia
- Improvement included decreases in left ventricular end diastolic volume (LVED) and in left ventricular end systolic volume (LVES) yet with no change in SV
- Maintained SV in the face of declining LV size

Caradon THERAPEUTICS

# Native UCN2 agonist was clinically validated by Johnson & Johnson in heart failure

## J&J Phase 1a Clinical Trial

- Healthy volunteers (n=30)
- No safety or adverse reactions
- behaved as seen in healthy dogs

## J&J Phase 1b Clinical Trial

- Patients (n=8) with stable HF (LVEF ≤ 40%)
- 3 consecutive (rising dose) 2.5-hour infusions of SCP resulted in improved cardiac output (CO) and LVEF
- No change in heart rate or blood pressure

Olson, A *Eur. Heart J.* 2012 33 805-806

## J&J Phase 2a: Patients (n=62) with HF (LVEF ≤ 35%)

- Patients were instrumented with a pulmonary artery catheter and randomly assigned (ratio 3:1) to receive 3 consecutive (rising dose) 1-hour IV infusions of CRF2 agonist or placebo
- Showed statistically significant increases in Cardiac Index (CI) and reduction in systemic vascular resistance were observed at the two top doses without significant changes in HR or systolic blood pressure (SBP)
- After 21 hours infusion, trend detected showing continued increase in CI and continued reduction in capillary wedge pressure

Gheorghiade, M *Eur. J. Heart Failure* 2013 15 679-689

Caradon THERAPEUTICS

# Overview of current and experimental drug therapies for human HF

| | Therapeutics | Mechanism of Action | Drugs | ROA | Effect on Heart |
|---|---|---|---|---|---|
| | **CARE110 (Caradon) (R&D/novel inotrope)** | **CRF2 agonist** | **PASylated® CRF2 Agonist Long-acting** | **>1x weekly SC** | **Improved heart performance without increase in O2 consumption, BP, or HR** |
| **Approved Generics** | B-blocker approved for HFrEF | β adrenergic receptor antagonists | bisoprolol, carvedilol, metoprolol, nebivolol | 1–2x daily small molecule | Decrease load on heart and heart rate |
| | ACEi / ARB Approved for HFrEF | Inhibition of angiotensin II synthesis or angiotensin receptors | captopril, enalapril, lisinopril, ramipril, trandolapril, irbesartan, valsartan, losartan candesartan | 1–2x daily small molecule | Decrease load on heart, reduction in blood pressure and improved diuresis |
| | MRAs approved for HFrEF | Aldosterone receptor antagonists | eplerenone, spironolactone, potassium canrenoate | 1–2x daily small molecule | Decreased load on heart and improved diuresis |
| | Diuretics Approved HFrEF | diminishing sodium reabsorption at different sites in the nephron | Bumetanide, furosemide, hydrochlorothiazide, metolazone, torsemide | 1–2x daily small molecule | Decrease load on heart |
| **Approved New** | ARNi Approved for HFrEF | Neprilysin inhibitor / angiotensin receptor blocker | sacubitril/valsartan (Entresto™) | 1x daily small molecule | Prevents breakdown of endogenous hBNP, decrease blood pressure, and improved diuresis |
| | sGC activator standard of care HFrEF | intracellular cGMP levels | Vericiguat (Verquvo®) | 1x daily small molecule | Increased levels of intra cellular cGMP resulting in decrease blood pressure and improved diuresis |
| | Gliflozines Approved HFpEF/HFrEF | SGLT2-inhibitors | dapagliflozin, empagliflozin | 1x daily small molecule | Diuretic and glucose elimination and AMP kinase activation |
| **R&D** | Positive Inotrope (R&D) | Activation of myosin and increased ATP hydrolysis | omecamtiv mecarbil | 1x daily small molecule | Limited Improved heart performance |
| | Gene Therapy (R&D) | Myocardial restoration of gene expression | AAV/SERCA2a, Ad5.hAc6 | Single IV administration | Improved heart performance without increasing myocardial energy demands |
| | Biologics (R&D) | Inhibition inflammatory pathways | Various inflammatory targets | IV and SC | Anti-inflammatory and anti-fibrosis |

Note: Additional HF therapies and approaches include combination drug therapies or phenotype and biomarker focused approaches, non-pharma interventions like LVADs/CRT

Caradon THERAPEUTICS

# Cardiovascular-focused deals and investor exits (through Q4 2023)

| Company | Compound | Target Indication | Purchased By | Dev Stage | Year | Deal Value |
|---|---|---|---|---|---|---|
| **CinCor Pharma** | baxdrostat | Resistant hypertention | AstraZeneca | Phase2 | 2023 | $1.8B |
| **Acceleron** | Mulitple PAH drugs | Pulmonary arterial hypertension | Merck | Commercial | 2021 | $11.5B |
| **Corvidia Therapeutics** | anti-IL6 antibody | Cardio Renal Syndrom | Novonordisk | Phase 2 | 2020 | $2.1B |
| **The Medicines Company** | cholesterol-lowering siRNA (inclisiran) | atherosclerotic cardiovascular disease; hypercholesterolemia | Novartis | NDA pending | 2020 | $9.7B |
| **Arena Pharmaceuticals** | Multiple CV drugs | Chronic HF | Pfizer | Commercial | 2020 | $13.1B |
| **Bayer (US rights only)** | soluble guanylate cyclase stimulator (Vericiguant) | Chronic HF and pulmonary arterial hypertension | Merck | Phase 3 | 2019 | $1B |
| **MyoKardia** | multiple CV drugs (mavacamten) | obstructive hypertrophic cardiomyopathy (“HCM”) | BMS | NDA pending | 2019 | $9.7B |
| **Staten Biotechnology** | anti-apoC3 antibody | Hypertriglycerdemia | Novonordisk | Pre-clinical | 2018 | $485M |
| **Cardioxyl Pharmaceuticals** | Novel nitroxyl prodrug | Acute decompensated HF | BMS | Phase 2 | 2015 | $2.0B |
| **ZS Pharma Inc.** | potassium-binding compound ZS-9 (sodium zirconium cyclosilicate) | treatment for hyperkalaemia | AstraZeneca | NDA | 2015 | $2.7B |
| **Omthera** | omega-3-carboxylic acid (Epanova) | hypertriglyceridemia | AstraZeneca | Phase 3 | 2013 | $443M |
| **Novacardia** | adenosine A1 receptor antagonist | Congestive HF | Merck | Phase 3 | 2007 | $350M |
| **Scios** | Endogenous human brain natuiretic peptide (neseritide) | Acute decompensated HF | J&J/Janssen | Commercial | 2003 | $2.4B |

**Appropriately de-risked CV assets are highly attractive as big pharma acquisitions and provide significant returns for investors**

Caradon THERAPEUTICS

# Overview and Takeaway of Caradon's Innovative Approach

- As pioneers of long-acting peptides for cardiometabolic diseases, Caradon presents a unique opportunity in large market drug development
- The team provides very unique expertise in peptide agonist development, as well as proven business success across all stages of product development
- There is a large unmet need for a heart failure drug that can restore cardiac function without increasing energy demands
  - Proof of concept already exists and MOA is derisked
  - Caradon's technology builds upon this by allowing for weekly dosing
- The technology has utility across multiple large therapeutic areas and markets.

Caradon
THERAPEUTICS