

# **ViCardia Therapeutics, Inc.**

## **Category:**

Best Startup

## **Company Name:**

ViCardia Therapeutics, Inc.

## **Turnover and/or Funding:**

Dilutive Financing to Date

Founders Common - \$500K

Series A Round - \$3.5M

Non-Dilutive Funding to Date

\$14.5M in licensing proceeds from Schering Plough, prior research conducted by Pericor Therapeutics and Gensia Pharmaceuticals

Initiating \$35M Series B Round in Q3 2024

ViCardia anticipates achieving the following milestones post financing:

- Complete Phase 2 clinical trial of GP-531 in 255 patients at 52 research sites (12-15 months from 1st patient treated to final data read-out)
- Complete new solid oral formulation for daily maintenance dose and other innovations and indications
- Pursue robust patent program including completing patent filings for new innovations and indications

## **Sub-Category:**

Biotechnology

## **Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):**

ViCardia Therapeutics is developing a first-in-class treatment for Acute Heart Failure

syndrome. AHF represents the highest unmet medical need in Cardiology today.

ViCardia is a Delaware corporation, founded in 2018, and is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapies for treating cardio-renal syndrome, metabolic disorders and neurological disorders involving mitochondrial dysfunction.

ViCardia is led by a highly experienced management team, board of directors and board of scientific advisors with deep experience in treating heart failure and conducting cardiovascular research.

In 2018, ViCardia acquired the extensive patent portfolio for three compounds known as Adenosine Regulating Agents (ARAs) and Adenosine Mono-Phosphate Kinase (AMPK) agonists from Pericor Therapeutics, Inc. ViCardia's lead asset, GP-531, is a potent, long-lasting, mitotropic agent, administered as an infusion therapy, that targets mitochondrial dysfunction identified as the underlying cause of heart failure. The therapeutic indication for GP-531 at the time of first market entry will be Acute Heart Failure, for which the clinical need is highest.

ViCardia has assembled a formidable, global patent platform consisting of 40 patents including composition of matter and method of use, formulation and composition. There are 8 additional patents pending covering new discoveries and treatment indications.

Over the past 30 years, Acute Heart Failure is the only category of cardiovascular disease with rising prevalence (>6.5 million patients in the US, >70 million worldwide), incidence, hospitalization rate, and total burden of mortality. Currently there is no therapy addressing the mortality risk of the patient hospitalized with Acute Heart Failure. Even with the very best of modern therapy, hospitalization for AHF is still associated with high 30-day, 60-day and 1-year mortality rates.

Despite more than 30 years of research and development, the primary pharmacological therapies for Acute Heart Failure are still:

- Intravenous Loop Diuretics as the primary therapy for most patients admitted with AHF to decrease venous congestion and fluid volume overload
- Intravenous Vasodilators reducing fluid volume overload
- Calcitropes - inotropes that improve cardiac function by altering myocardial calcium transients (generally discouraged due to serious adverse side effects)

GP-531 represents a major advance in technology to treat acute heart failure – the first in decades.

Main Funding to Date:

Dilutive Financing to Date:

Founders Common - \$500K

Series A Round - \$3.5M provided by two well-known venture capital funds, two family offices and high net worth individuals

Non-Dilutive Funding to Date:

\$14.5M licensing proceeds from Schering Plough, prior research conducted by Pericor Therapeutics and Gensia Pharmaceuticals.

## **History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):**

GP-531 is a second-generation member of a novel new class of agents termed “adenosine regulating agents” (ARAs) whose principal effects are mediated by augmentation of local endogenous adenosine levels. Its effects are not mediated by conversion of the drug to adenosine or any direct activity at the adenosine receptors. Importantly, the mechanism of GP-531’s action is event-specific and site-specific, whereby local adenosine levels are increased only in areas of ischemia/hypoxia where adenosine triphosphate (ATP), the precursor of adenosine, undergoes net catabolism. The significance of these observations is that therapeutic levels of GP-531 are pharmacologically silent in normally metabolizing tissue, resulting in no direct cardiac or systemic hemodynamic effects. A number of preclinical studies have demonstrated GP-531’s cardioprotective activity mediated by its effects on endogenous adenosine levels.

GP-531 has been shown to improve hemodynamics in a canine model of advanced chronic heart failure without chronotropic effects and without increasing myocardial oxygen demand. No episodes of hypotension, arrhythmias or death occurred in GP-531-treated dogs in these studies. GP-531 treatment also resulted in decreased plasma levels of BNP and Troponin.

GP-531’s cardioprotective properties suggest its potential to alleviate myocardial injury and improve cardiac function to improve the prognosis of hospitalized HF subjects.

In addition, GP-531, like its parent compound, AICAR, is an Adenosine Monophosphate-activated protein kinase (AMPK) agonist which regulates various physiological and pathological cellular events of great importance for the maintenance of cardiac function. These include the control of both metabolic and non-metabolic elements targeting the different cellular components of cardiac tissue, i.e.,

cardiomyocytes, fibroblasts, and vascular cells. The description of the multifaceted action of the two AMPK catalytic isoforms,  $\alpha 1$  and  $\alpha 2$ , AMPK gamma subunit, emphasizes the general protective action of this protein kinase against the development of critical pathologies like myocardial ischemia, cardiac hypertrophy, diabetic cardiomyopathy, and heart failure.

Once activated by energetic stress, AMPK modulates a variety of physiological processes in order to maintain sufficient ATP levels for sustaining the contractile function and membrane ionic gradients that are both important for the preservation of cell function and viability. AMPK has also an important action in regulating mitochondrial reactive oxygen species (ROS) production. AMPK is activated during low-energy cellular states, such as myocardial ischemia. It preserves the energetic equilibrium by promoting glucose uptake and glycolysis, while decreasing energy-consuming processes, through the various mechanisms described above. The beneficial role of AMPK activation in the ischemic heart has been clearly demonstrated in various mouse models where AMPK activation has been genetically impaired.

Hypertrophy and HF are associated with energy depletion (Neubauer 2007), and this has sparked extensive interest in the actions of AMPK and its potential as a novel target to prevent HF development (Beauloye et al. 2011).

As a conclusion, it appears that GP-531 as an AMPK agonist may play a decisive role by halting the progression of cardiac hypertrophy to heart failure. The cardioprotective effects of AMPK might be conferred via actions that extend beyond its metabolic control, such as effects on neovasculogenesis, autophagy, oxidative stress, fibrosis, and others.

ViCardia has several academic collaborations including the Gladstone Institutes in San Francisco, the Henry Ford Institute in Detroit, the Mayo Foundation and Clinic, the University of Pittsburgh, and Oxford University.

## **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

ViCardia is developing GP-531, which acts as an AMPK agonist and an ARA targeting mitochondrial dysfunction as the underlying cause of chronic heart failure that ultimately progresses to acute heart failure. Abnormalities in cardiac metabolism, such as a lack of ATP-ADP catabolism, causes mechanical failure of the heart.

In addition to its metabolic effects, AMPK regulates mitochondrial biogenesis, autophagy, cell polarity, cell growth and proliferation. Severe energetic stress is harmful to mitochondria and, over time, all mitochondria become damaged and need to be replaced. The metabolic changes observed in the mitochondria are considered a

critical landmark in the development of CHF and, ultimately, to AHF.

The principal effects of GP-531 is mediated by the localized augmentation of endogenous adenosine. Endogenous adenosine is a natural defense against myocardial injury via a number of mechanisms. At the molecular level, endogenous adenosine acts as a retaliatory metabolite that counters ATP catabolism and depletion, and as such, acts as a key regulator of cellular energetics. At the cellular level, endogenous adenosine protects the cell from multiple pathways of injury, including inflammation, apoptosis and necrosis, all of which are major contributors to myocardial injury and global myocardial dysfunction

Therefore, mitochondrial pathophysiology provides an important therapeutic target for reviving the contractile function of the myocardium, reversing events leading to AHF.

ViCardia proposes conducting a Phase 2, multicenter, randomized, double-blind, placebo-controlled, dose-escalation study to evaluate the safety, tolerability, hemodynamic and symptomatic effects of GP-531 in subjects hospitalized for AHF. ViCardia intends to show in the Phase 2 that GP-531 increases survival in patients hospitalized for AHF, reduces incidences of rehospitalization, increases long term health, and improves quality of life for the AHF patient.

Hospitalization for AHF is one of the most important predictors of mortality and readmission in subjects with chronic HF. Over 1 million hospitalizations with a primary diagnosis of HF occur in the U.S. each year. As a diagnosis at hospital discharge, AHF has tripled over the last 3 decades. This trend will likely continue due to an aging population, improved survival after myocardial infarction (MI), and better prevention of sudden cardiac death.

Management of AHF is challenging given the heterogeneity of the patient population, absence of a universally accepted definition, incomplete understanding of its pathophysiology and lack of robust evidence-based treatment guidelines. The majority of subjects appear to respond well to initial therapies consisting of diuretics and vasoactive agents. However, post-discharge mortality still reaches 20% and re-hospitalization rates reach 30% within 3 to 6 months.

New approaches have targeted symptoms, hemodynamics, or specific biochemical pathways of the disease process. Despite the efficacy of many therapies for patients with CHF, hospital admissions for AHF continue to increase and no new therapies have improved clinical outcomes.

Therefore, therapies that modulate cardiac metabolism, and increase ATP output, are pivotal in effectively addressing CHF and AHF, in particular.

There is a major unmet need for increased individualized in-hospital management of

AHF, including treatments targeting the causative factors, and continuation of treatment after hospital discharge to improve long-term outcomes.

**Please provide appropriate references (PubMed, Abstract, Website):**

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