COMPANY UPDATE

CERENO SCIENTIFIC

A RARE OPPORTUNITY IN CARDIOVASCULAR DISEASES

INTRODUCTION

INTRODUCTION

Cardiovascular diseases (CVD) are the most common cause of death in the world. An estimated 17.9 million people die annually from CVD, and World Health Organization forecasts suggest that 22.2 million people will to die from CVD by 2030. With an increasing number of people suffering from severe conditions resulting from CVD in combination with insufficient treatments, the medical need to improve the situation for these patients is growing.

CVD is also causing significant societal costs, in the EU the present annual bill has been estimated at USD 210 billion and USD 555 billion per year in the US. These numbers are expected to double by mid-2030.

Cereno Scientific's ambition is to find new therapies within this large field of common and rare CVDs, using an epigenetic modulation platform based on histone deacetylase inhibitors (HDACi).

One of the most common epigenetic modulators is a class of enzymes called histone deacetylases (*HDACs*). HDACs are found throughout the body in most cells, and, when stimulated, they can lead to changes to how an individual's DNA is read within the cells, which can affect key cellular mechanisms, thus increasing the risk of disease.

Like with gene editing, scientists have found ways of regulating some disease-causing epigenetic changes as a form of therapy. Compounds called HDAC inhibitors are epigenetic modulators with a whole spectrum of potential disease-modifying effects.

HDACi has thus attracted attention from many pharmaceutical and biotech companies in different areas; Cereno Scientific is the first to explore the commercial possibilities of epigenetic modulation in CVD.

Founded in Gothenburg

Founded in 2012, Cereno Scientific's drug candidate *CS1* was based on the research by Professor **Sverker Jern** and his team at the **Wallenberg Laboratory, Sahlgrenska Akademin** at **University of Gothenburg**.

In 2016, Cereno stepped into collaboration with **Galenica**, an established pharmaceutical development company. The aim of this discovery journey was to create a novel formulation of VPA, a promising HDACi, that would allow using smaller drug doses for better safety and induce drug release in the human body only in the early morning hours for optimal therapeutic effect. The joint effort resulted in an innovative new asset that is known today as CS1, Cereno's lead candidate.

In 2016, the company was listed on the marketplace now known as **Spotlight Stock Market.**

Widened indication potential after phase I

Further preclinical studies eventually took CS1 into clinical phase I in 2017. The phase I results showed that CS1 demonstrated good safety and tolerability, that it significantly reduced a suppressor of the local fibrinolytic system, PAI-1, and showed no problems with bleeding.

In 2018, the final phase I results were published, giving Cereno Scientific the opportunity to prepare for a phase II with CS1.

INTRODUCTION

During spring 2019, the company's then newly formed Scientific Advisory Board (SAB) identified several new promising areas for CS1. The company saw potential in both common and rare CVD, and, given the specific properties of CS1, Cereno Scientific filed for *orphan drug designation* (ODD) with the **US FDA** for CS1 in pulmonary arterial hypertension (PAH). This is a rare, progressive disease characterised by high blood pressure in the pulmonary arteries.

In parallel, the company planned a phase II trial intended to be carried out in Russia and Bulgaria with the aim to prevent venous thrombosis in patients undergoing elective orthopaedic surgery. The trial was scheduled to begin by mid 2020, but in late March, it was postponed due to the COVID-19 pandemic.

The ODD offers strategic benefits and opportunities

The decision to suspend the phase II trial in venous thrombosis coincided with the FDA granting CS1 ODD-status for PAH.

The intention of an ODD is to give biotech and pharmaceutical companies incentives to develop new therapies in rare diseases of significant medical need.

Benefits include among other things, regulatory fee waivers, eligibility for research grants and tax credits for clinical trial costs. An approved orphan drug is also granted seven years of market exclusivity in the US and 10 years in Europe.

Given the prospects at hand, Cereno Scientific has now decided to revise its clinical strategy to initially focus on CS1 in PAH. A phase IIa trial in PAH is planned to start in the first half of 2021.

During spring 2020, the company also appointed a new scientific advisor, internationally renowned Dr **Raymond L. Benza**, Professor of Medicine and Director of the Division of Cardiovascular Medicine at **Ohio State University Wexner Medical Center**. Dr Benza is a leading expert in CVD with extensive experience in major clinical studies of new therapies. PAH is one of his primary clinical interests, and he is expected to contribute greatly to Cereno Scientific's future advancement of CS1 in PAH.

Paving the way for future indications

As mentioned, Cereno Scientific's SAB identified together with Cereno's scientists the use of the candidate in common cardiovascular conditions related to fibrosis and inflammation such as atrial fibrillation, heart failure and chronic kidney disease within the field of epigenetic modulation based on the HDAC inhibitory effect of CS1. Cereno Scientific will continue to develop their new chemical entities (NCEs), securing a potential beyond CS1.

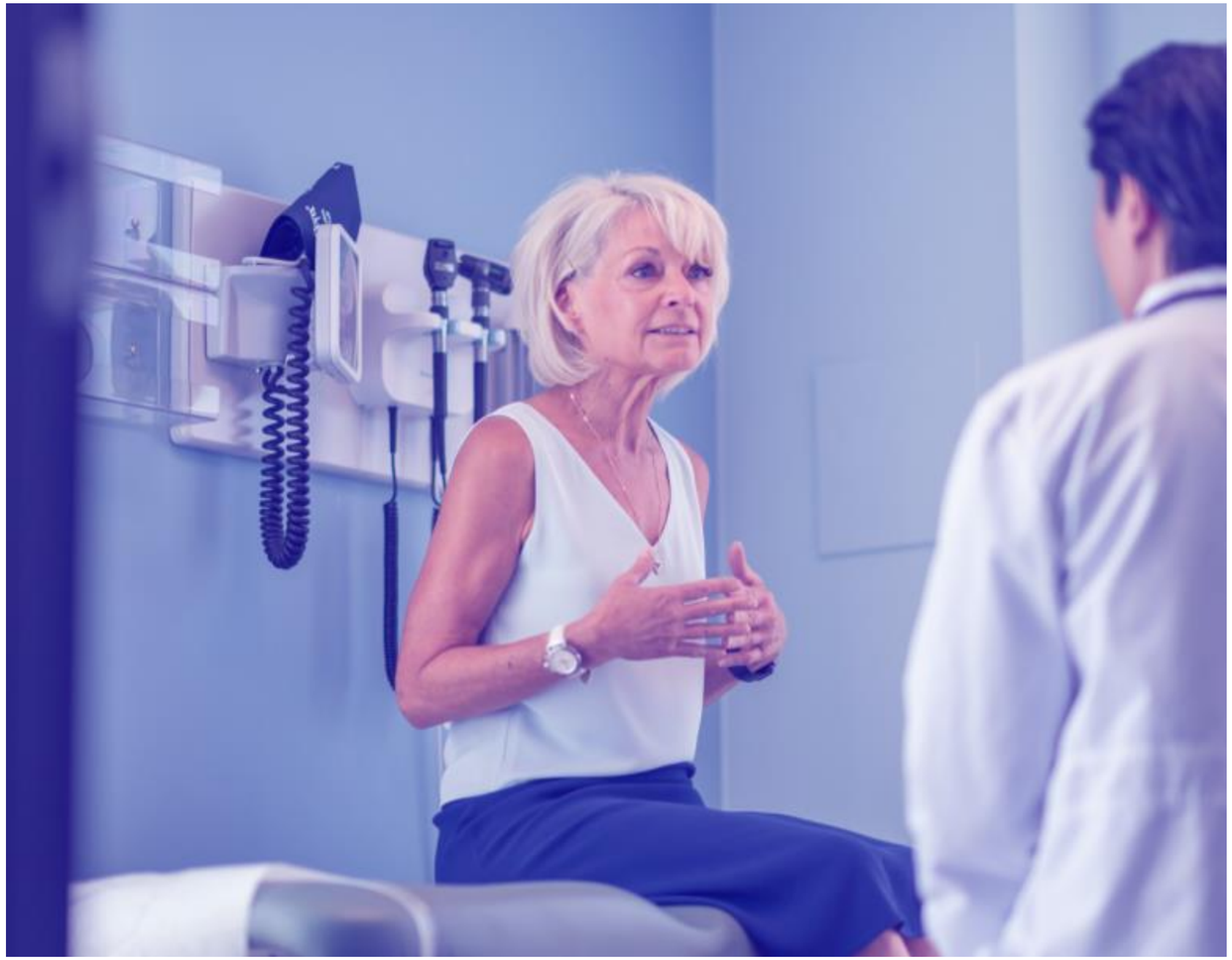
However, the main focus for Cereno Scientific at the moment is the clinical development of CS1 in rare disease PAH and the first step in validating its epigenetic modulation platform in CVD patients.

UPCOMING TRIGGERS

UPCOMING TRIGGERS

Key milestones

- Initiating the process to file for an Investigational New Drug (IND) application to the FDA for CS1 in PAH – year-end 2020
- Start of the clinical phase IIa trial with CS1 in PAH – first half of 2021
- Advancement of new chemical entities (NCEs) program



THE COMPANY IN BRIEF

THE COMPANY IN BRIEF

Cereno Scientific was founded in 2012 by Niklas Bergh, Sverker Jern and Pia Larsson and is based on research from the Wallenberg Laboratory, Sahlgrenska Academy at the University of Gothenburg.

Cereno Scientific is headquartered at the **AstraZeneca BioVentureHub** in Mölndal, Sweden. In May 2020, the company opened a new office located at Kendall Square in Boston, Massachusetts, US.

Presence at Kendall Square and **Cambridge Innovation Center** is a strategic advantage with closeness to several of the company's scientific advisors, leading research institutions and the US being the largest market for CVD therapies in the world.

Market	Spotlight Stock Market	**Number of shares**	71 819 312
Ticker	CRNO B	**Share price 2020-10-13**	SEK 1.98
ISIN	SE0008241558	**Market cap 2020-10-13**	SEK 142 202 238

Owners as of 2020-08-31*	**No. of shares**	**Capital (%)**	**Votes (%)**
Sverker Jern	1 221 327	3,04	7,10
Niklas Bergh	1 195 123	2,97	6,99
Avanza Pension	2 544 935	6,33	5,45
Ivar Nordqvist	2 112 212	5,25	4,52
Jonas Faijerson Säljö	871 614	2,17	4,47
Björn Dahlöf	956 735	2,38	4,44
Myrlid AS	2 000 000	4,97	4,28
GU Ventures AB	1 556 497	3,87	3,33
Nordnet Pensionsförsäkrings AB	839 376	2,09	1,80
Sten R. Sörensen	785 407	1,95	1,68

*Owners prior to the directed share issue announced Sep 30, 2020. The new ownership is currently under registration at the Swedish Companies Registration Office and not yet known.

THE COMPANY IN BRIEF

Board of directors and management team

The founders are shareholders of the company, active as board members and as part of management, reflecting a long-term commitment of carrying out the company vision of *"…improving the health of cardiovascular patients worldwide by unlocking the potential of epigenetic modulation in rare and common diseases."*

The board members have extensive experience from research and pharmaceutical industry in various roles, contributing with their expertise and international network.

Management, lead by CEO **Sten R. Sörensen** since 2015, covers key competences to be able to advance, fund, protect and communicate the clinical and preclinical projects. Team is depicted on next page.

The team has a combination of expertise from all areas of drug development. From scientific research and medical expertise to business development, intellectual property rights, finance and communication, they form an experienced and skilled team to execute on the company strategy.

Board of Directors

Catharina Bäärnhielm
Chairman of the board

- Chairman since 2015
- Pharmacist, PhD in pharmacokinetics and drug metabolism
- Experience from all phases of drug development
- Board member GU Ventures
- Prev. VP Global project manager, AstraZeneca

Björn Dahlöf
Board member

- Board member since 2012
- M.D., Associate professor of cardiovascular prevention at Sahlgrenska Academy
- Experience as an advisor for small and large pharmaceutical companies in all phases of drug development

Jonas Faijerson Säljö
Board member

- Board member since 2012
- PhD in neurobiology and licensed pharmacist
- Senior IP Business Consultant and CEO of Synergon

Sverker Jern
Board member

- Board member since 2012
- Professor of cardiovascular physiology at the Sahlgrenska University Hospital
- Jern's research is the basis for Cereno Scientific's new treatment

Anders Svensson
Board member

- Board member since Oct 2018
- Licensed physician, medical doctor and lecturer with over 20 years of experience in academic medicine focusing of CVD
- VP clinical development of cardiovascular, Astra Zeneca

Klementina Österberg
Board member

- Board member since 2014
- CEO of GU Ventures, University of Gothenburg's holding company
- Significant experience within venture financing and business development

THE COMPANY IN BRIEF

Management team

Sten R. Sörensen
Chief Executive Officer

CEO since 2015
Head of International marketing operations: Monsanto Global Marketing Director of secondary prevention products, Cardiovascular AstraZeneca.

Daniel Brodén
Chief Financial Officer

Previous experience as a financial manager for GU Ventures portfolio companies and has worked as an auditor at Frejs Revisorer as well as at PwC Financial services.

Niklas Bergh
Chief Scientific Officer

Associate Prof in Experimental Cardiology at Sahlgrenska Academy. Specialist in cardiology and resident physician at Sahlgrenska University Hospital.

Björn Dahlöf
Chief Medical Officer

Associate Prof of CV prevention at Sahlgrenska academy with 35 years of experience as a physician
Extensive CV research and drug development experience.

Jonas Faijerson Säljö
Chief Intellectual Property Officer

PhD in Neurobiology and a licensed pharmacist with a research background in the stroke area with wide-ranging experience in the commercialization of medical innovations. Senior IP Business Consultant and CEO of Synergon AB.

Anna Leitgeb
Director Regulatory Affairs

PhD in infectious diseases from Karolinska Institute. Extensive expertise in regulatory affairs and experience from research and drug development, and global project management. Currently employed by NDA Regulatory Services AB.

Tove Bergenholt
Director Communications & IR

Specialized in communications, IR and marketing activities in public biotech companies headquartered in the Nordics. Previous experience in global healthcare PR for AstraZeneca, Merck KGaA and Bayer. Currently employed by Monocl Strategy & Communication.

Jan-Peter Idström
Senior Director Development

PhD in Biochemistry extensive experience of R&D for gastrointestinal and thrombosis/ hemostasis products.
Has led Clinical Pharmacology and Experimental Medicine units at AstraZeneca.

Paula Salme Sandrak
Project Director

Specialized in project management and business analysis. Experience from biopharma, life science consulting and digital health companies in Sweden, UK and Germany. Trained in gene technology and bioentrepreneurship. Currently employed by Monocl Strategy & Communication.

THE COMPANY IN BRIEF

Scientific Advisory Board

Cereno Scientific has been able to attract internationally renowned experts and key opinion leaders to their scientific advisory board.

The members of the SAB are actively working with the company's clinical and preclinical programs, validating Cereno Scientific's epigenetic modulation technology in CVD.

However, Cereno Scientific's network is not limited to the SAB and reaches out to many of the leading research institutions in the field that are based in the US and elsewhere.

World leading expert in PAH

In connection with the ODD for CS1 in PAH earlier this year, Cereno Scientific recruited an additional top-level scientific advisor in Dr **Raymond L. Benza**, professor of Medicine and Director of the Division of Cardiovascular Medicine at the **Ohio State University Wexner Medical Center** in Columbus, US.

PAH is among Dr Benza's primary clinical interests and he has also participated in major clinical studies of new therapies and for the treatment of heart failure and PAH, among other diseases. He is a funded investigator for the **National Institutes of Health** and the **American Heart Association** for his work in PAH focusing on risk stratification, pharmacogenomics and new device therapies for PAH.

Scientific Advisory Board

Dr. Bertram Pitt, Chairman
Prof Em in Medicine, University of Michigan School of Medicine

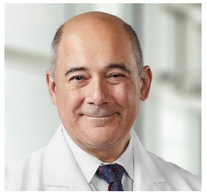
Dr. Deepak Bhatt
Prof of Medicine, Harvard Medical School

Dr. Gunnar Olsson
MD, PhD in Medical Sciences, vast experience from pharmaceutical development, Karolinska Institute

Dr. Gordon Williams
Prof of Medicine, Harvard Medical School

Dr. Faiez Zannad
Prof of Therapeutics and Cardiology, Université de Lorraine

Scientific Advisor



Dr. Raymond L. Benza
Professor of Medicine, Wexner Medical Center
Ohio State University

HARVARD MEDICAL SCHOOL

Karolinska Institutet

University of Michigan Medical School

UNIVERSITÉ DE LORRAINE

THE OHIO STATE UNIVERSITY

BUSINESS MODEL

BUSINESS MODEL

Cereno Scientific aims to become a leader in epigenetic modulation within common and rare cardiovascular diseases. Based on research from University of Gothenburg, the company has been developing a pipeline of HDAC inhibitors addressed for different conditions associated with cardiovascular diseases. The lead candidate CS1 is a new formulation of valproic acid, with a mechanism of action proven in preclinical studies to have the ability to balance the level of t-PA and PAI-1.

For more than 50 years, VPA has been a well-established treatment for epilepsy and a known HDAC inhibitor. Preclinical scientific evidence accumulated over the years suggests that epigenetic HDACi modulation with CS1 has several interesting properties i.e. being anti-thrombotic, anti-inflammatory, anti-fibrotic and blood pressure-reducing. There are also epidemiological studies to support reduction in stroke and myocardial infarction (MI).

VPA, t-PA and PAI-1

Cereno Scientific has found a way to harness the strengths of VPA – their lead candidate CS1 is a novel formulation of VPA – which has in *in vitro* studies, animal models, and human physiological studies showed the ability to stabilize the body's own fibrinolytic system by modulating two proteins involved in clot formation: increasing the storage of t-PA in the vessel wall and a reduction of PAI-1, an inhibitor of t-PA, circulating in the blood.

The protein t-PA is typically released in the blood vessels from the endothelial cell wall during an injury to avoid an occlusive build-up from blood clots. Meanwhile, PAI-1 is a circulating protein that blocks the action of t-PA. In healthy individuals, the two factors balance each other out, but in individuals at risk of thrombosis, the balance shifts and the risk of thrombosis is increased.

Successful phase I trial

CS1, unlike currently available therapies for thrombosis prevention (*Warfarin, Heparin* or *NOACs*), promises to be able to prevent thrombosis with minimal risk of bleedings. The phase I study confirmed the safety and tolerability of CS1 and the desired plasma profile of VPA in healthy, slightly overweight volunteers treated with CS1.

The study also confirmed a significant reduction of PAI-1 in response to CS1. This result links to the beneficial effects of VPA supported by several epidemiological studies that show reduction of stroke and MI in VPA-treated patients.

BUSINESS MODEL

Epigenetic modulation

Fibrosis can affect nearly all tissues of the body; it is a type of healing process that normally occurs during an injury, but could sometimes go out of control and become chronic and detrimental. If the injury becomes chronic, fibrotic tissue accumulates, leading to, e.g. pulmonary fibrosis, cardiac fibrosis, or hepatic cirrhosis, to name some of the most common, all of which could become fatal. In fact, as a whole, fibrosis is associated with 45 per cent of deaths in the western world.

Scientists have found evidence suggesting that fibrosis is associated with epigenetic changes and that epigenetic modulation with HDAC inhibition could play a major role in preventing and treating fibrosis. This has led researchers to take an in-depth look at the therapeutic effects of HDAC inhibition in the area of fibrosis.

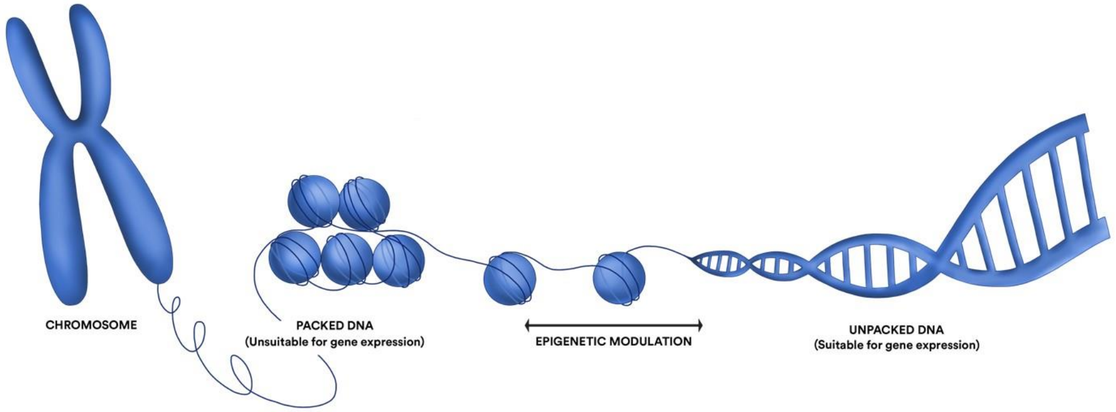


Illustration of epigenetic modulation.
Source: Cereno Scientific

As neatly summarized in a review article from 2016, VPA has been shown to have both preventive and therapeutic effects across a range of fibrosis-affected tissues in vital organs such as the heart, the lungs, the kidneys and the liver. There has been a growing interest in VPA, since it is a well-tolerated HDAC inhibitor with extensive clinical documentation suitable for long term treatment.

What is more, accumulating evidence has come out showing how epigenetic modulation through HDAC inhibition with VPA could be used as a disease-modifying therapy for treating a rare disease like Pulmonary Arterial Hypertension (*PAH*). For this disease, the anti-thrombotic, anti-inflammatory, anti-fibrotic and pulmonary pressure-reducing effects of CS1 are relevant.

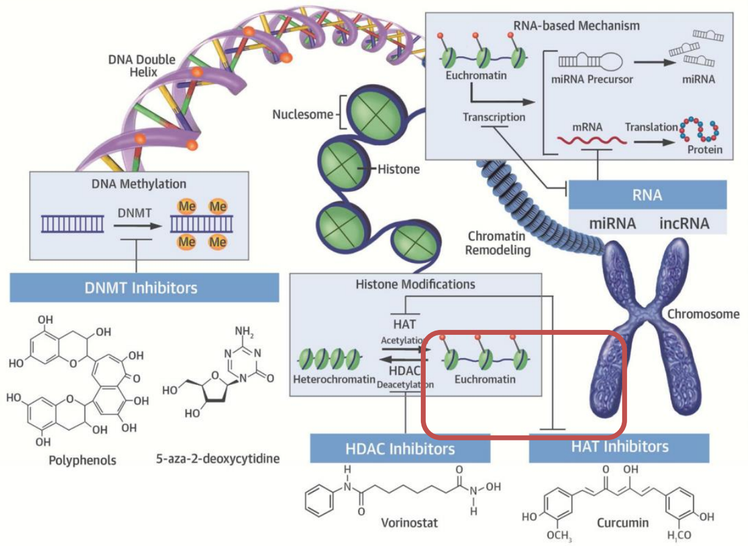


Figure. Potential therapeutic epigenetic targets in cardiovascular disease examples of targeting epigenetic mechanisms in CVD.

Possible targets include modifying DNA methylation, changing the acetylation or deacetylation of histones, and miRNA or lncRNA modifications. DNMT = DNA methyltransferase; HAT = histone acetyltransferase; HDAC = histone deacetylase; lncRNA = long noncoding RNA; miRNA = microRNA.

BUSINESS MODEL

Cereno Scientific holds the epigenetic key to broaden its CVD vision

PAH is just one example of how fibrotic and thrombotic mechanisms are related. The implications for the benefits of CS1 go even deeper, especially with regard to cardiac fibrosis, where evidence points to the epigenetic remodelling properties of VPA, able to reduce atrial fibrosis as well as atrial thrombosis and delay incidence of atrial fibrillation.

This gives Cereno Scientific a clear path to expand its potential indications into atrial fibrillation, heart failure, kidney disease and beyond.

Validated by leading experts and lead by an experienced management team

Cereno Scientific has been able to attract world leading experts and key opinion leaders in CVD to actively support and advise the advancement of the clinical and preclinical programmes. The SAB played an important part in the company's decision over the new CS1 rare disease strategy and will also contribute with valuable advice in the ongoing projects.

Cereno Scientific's management is a combination of expertise from all areas of drug development. From scientific research and medical expertise to business development, IP and finance, they form an experienced team with an extensive track record from the life science sector.

ODD offers benefits and reduces risk

The FDA grants ODD to drugs and biologic products that are intended for the treatment of rare diseases or disorders that affect less than 200 000 people in the US. The intention is to facilitate drug development for rare diseases and encompasses several benefits to drug developers.

One of the most compelling features of an approved orphan drug is a seven-year market exclusivity in the US, which provides an additional security layer to protect the drug's market share once launched.

Further, the ODD status include FDA fee waivers, e.g. the New Drug Application fee, currently corresponding to a value of USD 2.9 million.

The company is also eligible for tax exemptions for clinical trial costs and can apply for research grants to fund the clinical studies. An approved orphan drug is also often associated with a price premium compared to other drugs.

Given these advantages, the ODD status significantly enhances the value of the project.

European ODD possibility

The FDA has, as mentioned already, granted CS1 ODD status for PAH in the US, and that could also be the case for Europe and the European Medicines Agency, **EMA**, should Cereno Scientific choose to apply. Both regulatory authorities have developed similar frameworks for motivating drug development in rare diseases.

In Europe, market exclusivity is ten years for an approved orphan drug, compared to seven years in the US. The medical need to find new PAH therapies is as urgent in Europe as in the US.

BUSINESS MODEL

Pulmonary Arterial Hypertension

Patients suffering from PAH are exposed to a progressive disease associated with poor quality of life and high mortality. Despite some recent treatment advances, PAH remains incurable, except for lung transplantation, which, for the majority of patients, is not available in time.

PAH is characterized by the remodelling of distal pulmonary arteries, leading to increased pulmonary artery pressure, fibrosis, inflammation and thrombosis. The condition can lead to poor oxygenation and fatal right heart failure (RVHF).

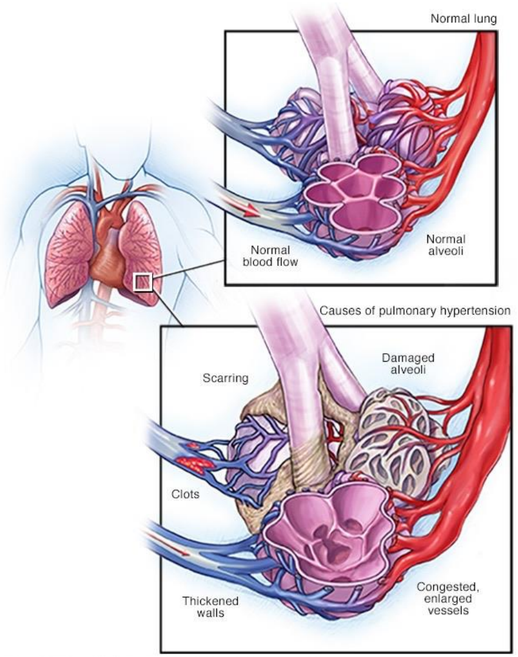
Around 1000 new cases are diagnosed with PAH in the US each year, according to data from National Institutes of Health. More than half of those that are affected, are attributed to idiopathic and heritable causes. Other cases are associated with drugs, toxins and diseases such as HIV and congenital heart disease. In certain regions schistosomiasis infections have been related to PAH.

Most cases are found among older adults over the age of 65 and more women than men are affected by PAH. Younger people and children can also suffer from PAH, seriously affecting their quality of life.

Current standard treatment consists of various drugs that have limited efficacy and often have to be combined with each other to reach acceptable treatment outcomes. The significant unmet treatment need for PAH is currently ready to be fulfilled; and that the FDA granted ODD status for CS1 in PAH is a validation of the fact that CS1 has fulfilled the criteria of showing potential to provide significant treatment benefits to PAH patients.

In earlier research, the active ingredient of CS1 has shown the potential to address known pathogenetic mechanisms of PAH thanks to having these attributes:

- Anti-fibrotic
- Anti-inflammatory
- Pulmonary pressure reducing properties
- Anti-thrombotic
  - restoration of t-PA depots locally in vessel walls, reduction of systemic PAI-1 and reduction of locally produced PAI-1.



Pulmonary Arterial Hypertension
Source: via Hibiscus BioVentures

BUSINESS MODEL

Projected timeline

Cereno Scientific plans to initiate a phase IIa study with CS1 in PAH during the first half of 2021, carried out in the US. Preparations include initiating the process to file for an Investigational New Drug (IND) application to the FDA for CS1 in PAH by the end of 2020.

Depending on the readout from this trial, the company has different options on how to proceed to the next phase – it is therefore difficult to assess the overall duration of the study period, although the company is expecting a readout from the phase IIa in 2022.

The company is planning a phase IIb trial shortly after the completion of the phase IIa study, including more patients and over a longer period of time. Depending on the outcomes of the trials, partnering and licensing discussions and other strategic decisions, Cereno Scientific has a long-term ambition of filing for marketing approval around 2027.

Exclusivities for CS1 in PAH based on potential approval in 2027

Market	EU28	US
Estimated market approval	2027	2027
CS1 treatment patent expiry	2038	2038
Orphan drug exclusivity	2037	2034
First year without exclusivity	2038	2038

“CS1 has to definitely be tested in PAH, it could be game-changing for patients.”

– Dr. Raymond L. Benza, Professor of Medicine and Director of the Division of Cardiovascular Diseases at the Ohio State University Wexner Medical Center and scientific advisor to Cereno Scientific.

POSITIONING AND COMPETITIVE LANDSCAPE

POSITIONING AND COMPETITIVE LANDSCAPE

Patients diagnosed with PAH are often started on a combination of different treatments. CS1 has shown potential to be addressing important pathogenetic mechanisms of PAH and could therefore be relevant both in combination with other therapies and as monotherapy.

PAH patients are often treated with combinations of different drugs to address the pathogenetic mechanism of the disease.

Combination treatments are becoming more adopted

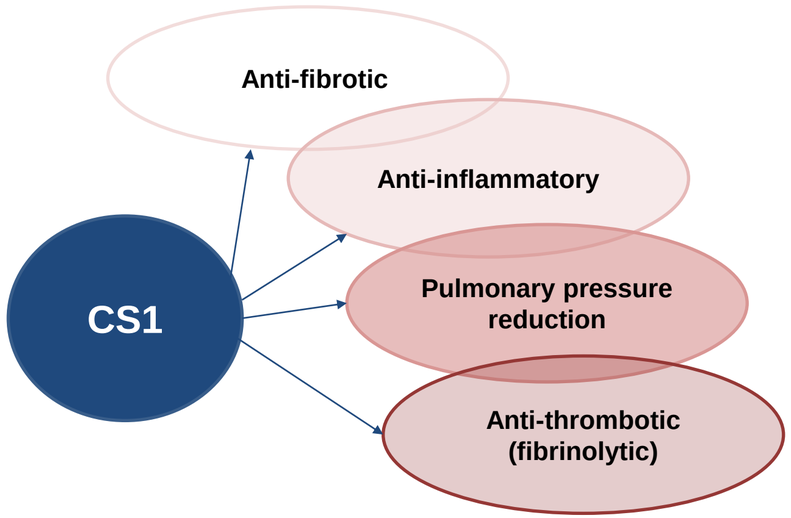
Early stage disease is treated with different classes of drugs following different pathways, such as endothelin receptor agonists (ERAs), PDE5 inhibitors (PDE5i) and depending on response and risk, further drugs can be added, e.g. prostacyclins (PCA) and soluble guanylate cyclase stimulators (sGC). Only patients with thromboembolism receive anticoagulants.

CS1 represent a new class of drugs to treat PAH

A key advantage of CS1 is the four-fold efficacy profile as described above and in the figure to the right. The candidate is able to address several known pathogenetic mechanisms of PAH.

Furthermore, CS1 is an oral, once daily treatment offering a convenient alternative for patients. It is proven to be safe and well tolerated, which indicates suitability as a potential long term therapy.

The four-fold efficacy of CS1



Source: Cereno Scientific

POSITIONING AND COMPETITIVE LANDSCAPE

Market potential

In 2019, the global PAH market was valued at 6.3 billion USD and is expected to reach 9.8 billion USD in 2027 with a CAGR at 5.6 per cent between 2020 – 2027 according to the American research firm **Grand View Research**.

In the table below, a number of the marketed drugs are listed; their class, name and how much they generated in sales in 2019. Some drugs are off patent, but still generate steady sales revenues.

Actelion, originally a swiss pharmaceutical company, acquired by **Johnson & Johnson** in 2017, is marketing a portfolio of PAH therapies. *Tracleer* and *Opsumit* have generated sales of 5 billion USD each since 2014.

Letairis/Volibris was approved by FDA in 2007 – an endothelin receptor agonist (ERA), once-daily oral treatment of PAH. The total sales in the US for Letairis has been reported to reach almost 6 BUSD in the 2010s, according to **Gilead Sciences**'s annual reports. The patent for Letairis expires in 2020.

Adempas is a drug commercialised by **Bayer** and approved by FDA in 2013 to treat PAH and chronic thromboembolic pulmonary hypertension (CTEPH) – a condition that is also characterized by hypertension in the pulmonary artery, but of different origin than PAH. Since approval up to 2019, Adempas has sold for 1.6 billion EUR globally, with the US market as an important driving force. The Adempas patent is valid until 2027.

The market for PAH therapies is growing steadily, and new therapies are constantly developed. Cereno Scientific and its SAB strongly believe that CS1 will be able to enter this fiercely competitive market and will help transform how PAH is treated in the future.

POSITIONING AND COMPETITIVE LANDSCAPE

Marketed drugs used in PAH treatment

Class	Name	Molecule	Company	Sales* 2019 (MUSD)	Patent expiry
ERA	Tracleer	bosentan	Actelion	321	Nov 2015
	Volibris/ Letairis	ambrisentan	GSK/Gilead	618	Dec 2020
	Opsumit	macitentan	Actelion	1327	Dec 2025
PDE5i	Revatio	sildenafil	Pfizer	22	Sep 2012
	Adcirca	tadalafil	Eli Lilly	107	Aug 2018
sGC stimulators	Adempas	riociguat	Bayer	418	Sep 2002
PCA	Uptravi	selexipag	Actelion	819	Oct 2026
	Remodulin	treprostinil	United Therapeutics	587	Jun 2018
	Tyvaso	treprostinil	United Therapeutics	416	Jan 2026
	Orenitram	treprostinil	United Therapeutics	225	Feb 2030

* Sales figures from annual reports

POSITIONING AND COMPETITIVE LANDSCAPE

Deals in the PAH space

Several deals in the PAH space have been struck during the past decade, particularly in recent years, indicating a growing interest for the area. Given the underlying medical need for new therapies, projected market growth, new deals are likely to be announced in the coming years.

An ODD status has historically been a value driver for licensing deals, which gives Cereno Scientific a good position in future negotiations.

Date	Licensee	Licensor	Candidate/drug	Phase	Region	Total deal value (USD)	Upfront (USD)
15 Nov 2018	United Therapeutics	Arena Pharmaceuticals	APD811	III	Worldwide	1.2 B	800 M
5 Dec 2017	Everest Medicines	Arena Pharmaceuticals	APD811	II	China, Hong Kong, Macau, South Korea	224 M	12 M
2 Oct 2017	Gossamer Bio	Pulmokine	GB002	I	Worldwide	303.5 M	5.5M
6 Jan 2017	VIVUS	Selten Pharma	VI0106	II	Worldwide	40 M	1 M
5 Jun 2014	Merck & Co	Bayer	Adempas	Marketed	Worldwide excl US	2.1 B	1 B
17 Feb 2010	Nippon Shinyaku	Actelion	Uptravi	II	Worldwide	50 M*	30 M

* Before the compound had an ODD

IP-SITUATION AND REGULATORY NOTICES

IP-SITUATION AND REGULATORY NOTICE

Cereno Sceintific's IP position encompasses patents protecting its discoveries regarding epigenetic modulation with HDACi, and the novel formulation of VPA, CS1.

Filing for a WO patent, means that the application is administrated by **World Intellectual Property Organization** (WIPO) to its member states. The company can thus reach several countries and regions with one filing. There are 184 member countries, including the US, China and many European countries.

Since there is no international patent, every region or country will grant the application in their own process. For instance, Cereno Scientific was granted a patent for its first patent family in Australia in March 2019, valid until 2032 with possibility to extend for a maximum of five years. Other processes are ongoing for the other patent families and several patents have already been granted in important jurisdictions, including in the US.

Orphan drug designation

On the 9 March 2020, the FDA announced that they had granted CS1 an orphan drug designation for the treatment of PAH in the US. The ODD status could also be filed for in Europe. The European Medicines Agency has a similar approach to similar approach to supporting rare disease drug development as the US FDA. Should Cereno Scientific be granted an ODD in Europe, the value of the project would instantly rise further in reflection.

Patent family number	Patent family	Status	Application filed	Estimated patent expiry
WO2012/120262	For the use of various HDACi to increase t-PA production	Granted	2011	2032
WO2016/055797	For the use of VPA to reduce PAI-1, including dosing, formulations and optimal efficacy	Granted	2014	2038
WO2017/175013	To expand protection around formulation and use of CS1	Pending	2016	

FINANCIAL STATUS

FINANCIAL STATUS

On September 30, 2020, Cereno Scientific announced new funding by a directed share issue of SEK 60 million and a loan facility of SEK 10 million. The funds will cover preparations for the upcoming phase IIa trial with CS1 in patients with PAH and pave way for future indications.

The directed offer included units consisting of two newly issued shares and two warrants, TO1 and TO2, with different subscription periods. The company will also issue warrants of series TO1 and TO2 to existing shareholders.

The subscription period for TO1 begins on the 15 September 2021 and would add SEK 98.4 million should the warrant be fully subscribed at the maximum subscription price SEK 2.84 per share.

The subscription period for TO2 starts 14 September 2022 and would potentially add SEK 114.8 million based on the maximum subscription price SEK 3.33 per share.

With the use of the proceeds from the directed issue and the loan financing, Cereno Scientific will be able to advance CS1 to the upcoming phase IIa trial. The warrants are intended to finance the completion of the phase IIa trial as well as to advance the company's preclinical pipeline.

With the ODD-status and financing in place for the initial phase IIa trial, Cereno Scientific makes an attractive target for other pharma and biotech companies for potential licensing and partnering deals. This type of discussions will probably be a more frequent activity in Cereno Scientific's board room as the project advances.

Added funding in 2020	**MSEK**
Rights issue	60
Loan facility	10

Potential funding		**Start of subscription period**
Warrant series TO1	98,4	15 September 2021
Warrant series TO2	114,8	14 September 2022

Financial calendar	**Date**
Interim report Q3 2020	19 November 2020
Year-end report 2020	25 February 2021

BIOSTOCK'S COMMENTS

BIOSTOCK'S COMMENTS

Cereno Scientific has followed the path of many other drug developers, a journey with significant risks at every stage of the process, e.g. funding risk, development risk, regulatory risk and competition from other projects, but with the possibility of great rewards if successful.

A drug is typically approved after 12-15 years of discovery studies, preclinical research, clinical phase studies and manufacturing challenges. Cereno Scientific's lead candidate has reached as far as clinical phase II. Only 1 of 5 000 compounds go all the way from discovery to the market, the probability for a phase I candidate to approval is 9.6 per cent according to data between 2006 and 2015. The likelihood for final approval is significantly improved when reaching phase II – 15 per cent for all candidates. For ODD candidates, the probability increases to 30 per cent.

When Cereno Scientific announced that they would postpone the start of its planned phase II study with CS1 in VTE due to the pandemic, the share price plummeted in disappointment of the delay.

However, since the announcement the CS1 rare disease strategy together with the new funding, the share price has recovered, implying a current market value of around SEK 140 million. Management, with extensive experience and depth in key competences, is poised to carry out Cereno Scientific's vision and take on the challenge to advance CS1 to the next phase.

Validation and guidance by leading external scientific experts together with the ODD in the US, are clear value drivers for the project. The revised clinical strategy for CS1 will reduce the overall risk and still preserve Cereno Scientific's long-term potential.

Approaching clinical phase II, potential partners and licensing deals will also come into play, although Cereno Scientific could choose to go to market in a rare disease on its own.

Although PAH is a rare disease, earlier approved drugs have generated sales in the scale of billions of USD, as CVD is one of the largest pharmaceutical markets. The underlying medical need is great and growing worldwide, PAH has no known cure and current treatments are insufficient.

The lead candidate CS1 has the potential to pave way for a new class of drugs in treating PAH, creating an opportunity to harvest a significant part of the market valued at almost USD 10 billion in 2027.

A successful candidate would validate Cereno Scientific's epigenetic modulation technology platform and would open possibilities for other applications in both rare and common CVD. For the longer term, herein lies an even greater value.

Key points

- ***A clear strategy for the lead asset CS1***
- ***Committed owners, skilled management and scientific advisors forms the foundation for continued strong execution and growth***
- ***Funding in place to initiate the next clinical phase***
- ***Large long-term potential in CVDs beyond PAH***

DISCLAIMER

This analysis is a Status Report by BioStock, conducted on commission by the analyzed company. BioStock's remuneration for the work has been agreed upon beforehand and is independent of the content and conclusions reached in the analysis. The content of this analysis is based solely on publicly available information gathered through research by the analyst from sources such as e.g. financial reports and statements, the company's web page, public presentations and in dialogue with representatives of the company's executive management. The information about the company was made available to the company for fact-checking and was published subsequent approval by the company. The analysis contains subjective assessments regarding future events and outcomes, which should be considered to render such assessments to be uncertain. Any valuation of the company, products and/or markets has been made by BioStock's analyst. The analyst does not own shares in the company. This analysis should not be considered as a recommendation or advice to invest in the company nor shall it be interpreted as financial advice of any sort. BioStock cannot and does not give any guarantees that the conclusions or forecasts presented in this analysis will be fulfilled. BioStock cannot be held responsible or liable for any damage, direct or indirect, caused by decisions made based on the information in this analysis. BioStock is not subject to the oversight of the Swedish financial authority Finansinspektionen and is thus not required to comply with the specific rules and guidelines that apply to analysis firms subject to the oversight of Finansinspektionen.

CONTACT

BioStock AB
Medicon Village
Scheeletorget 1
223 81 Lund
red@biostock.se

APPENDIX

ABBREVIATIONS

AF	Atrial Fibrillation
BPA	Balloon Pulmonary Angioplasty
CTEPH	Chronic Thromboembolic Pulmonary Hypertension
CVD	Cardiovascular Disease
DVT	Deep Vein Thrombosis
EH	Essential Hypertension
ERA	Endothelin Receptor Agonist
HDAC	Histone Deacetylase
HDACi	Histone Deacetylase inhibitor
IPF	Idiopathic Pulmonary Fibrosis
MI	Myocardial Infarction
NCE	New Chemical Entity
NOAC	Novel Oral Anticoagulant
ODD	Orphan Drug Designation
PAH	Pulmonary Arterial Hypertension
PAI-1	Plasminogen Activator Inhibitor-1
PCA	Prostacyclin Analog
PDE5i	PDE5 inhibitors, phosphodiesterase 5 inhibitors
PE	Pulmonary Embolism
PEA	Pulmonary Endarterectomy
PF	Pulmonary Fibrosis
PH	Pulmonary Hypertension
PoC	Proof of Concept
RD	Rare Diseases
RoA	Route of Administration
RVHF	Right ventricular heart failure
sGC	soluble Guanylate Cyclase
SPAF	Stroke Prevention in Atrial Fibrillation
t-PA	tissue Plasminogen Activator
VPA	Valproic Acid
VTE	Venuous Thromboembolism
WIPO	World Intellectual Property Organization