CiVi BIOPHARMA

Creating Novel **Oral**
Antisense Oligonucleotide
Therapies

CORPORATE PRESENTATION

June 2023

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INVESTMENT HIGHLIGHTS

CIVI 008, a novel oral PCSK9 with a targeted IND submission in 4Q'23, should be positioned to initiate a Phase 1/2a study in Atherosclerotic Cardiovascular Disease (ASCVD), an indication with multi-billion market potential.

CIVI 030, for which an NDA has been submitted to the FDA for the treatment of frostbite, **an orphan disease with no FDA approved treatments.**

We believe the patented oral delivery platform, COPE, is an enhancer of GI drug absorption, facilitating **oral delivery of oligonucleotide drugs,** and enables the efficient development of several product candidates.

Seasoned leadership team **with strong track record** in drug discovery, development and successful commercialization of therapies.

Multiple near-term clinical and regulatory milestones over next 6-12 months.

Existing Investors: **Boxer Capital, Roche Ventures, Tang Capital, RA Capital and a leading NYC-based biotechnology investment fund.**

EXPERIENCED MANAGEMENT TEAM

	**Shal Jacobovitz** **Chief Executive Officer**	• **30+ years experience in pharma industry leadership roles (Actelion U.S., F. Hoffman LaRoche, Abbott Canada, Nordic Labs & Marion Merrill Dow [now Aventis])** • **Former CEO of the American College of Cardiology (2013-2018)** • **Former President of Actelion US (2004-2013), acquired by J&J for $30B**
	**Henrik Oerum, MD, MSc** Chief Scientific Officer	• 25 years as biotech entrepreneur and pharma executive (Boehringer Mannheim & Hoffmann-la Roche) • Led development of LNA antisense drug platform at Santaris • Founder of CIVI Biopharma, Santaris Pharma & Exiqon
	**Chuck Shear, DrPH, FAHA, FACC** Chief Development Officer	• 30+ years experience in pharma industry in CV therapeutic area development leadership roles (Merck, Pfizer, CLS Behring) including lipid-lowering programs; statins, CETP, HDL infusion and PCSK9
	**Wade Benton, PharmD** Chief Development Officer at Civi orphan disease subsidiary, Eicos Sciences	• 20 years experience in drug development and academic research in Systemic Sclerosis, PAH, Cystic Fibrosis, Pediatric Critical Care • 15 years experience developing and commercializing prostacyclin analogs • Founder and CDO of Eicos Sciences, Inc
	**Kevin Christal** Chief Operating Officer	• 20 years experience in commercial operations and business development spanning numerous disease areas • 15 years experience developing and commercializing prostacyclin analogs • Co-founder and COO of Eicos Sciences, Inc.

DEVELOPMENT PIPELINE

Robust pipeline with mix of early and late-stage programs

Drug	Target	Rt of Admin	Indication	Development Stage				
				Discovery	Pre-clinical	Phase I/II	Phase III	NDA
CIVI 008	PCSK-9	Oral	Lipid disorders			Expected IND filing 4Q'23		
Iloprost (CIVI 030)	IP-Rec.	I.V.	Frostbite					Expected July'23 PDUFA date
COPE Platform	Numerous	Oral	Numerous large/small market; indications tbd					

CIVI 008

A long-acting, third generation PCSK9 in development for treatment of hypercholesterolemia and prevention of atherosclerotic cardiovascular disease (ASCVD)

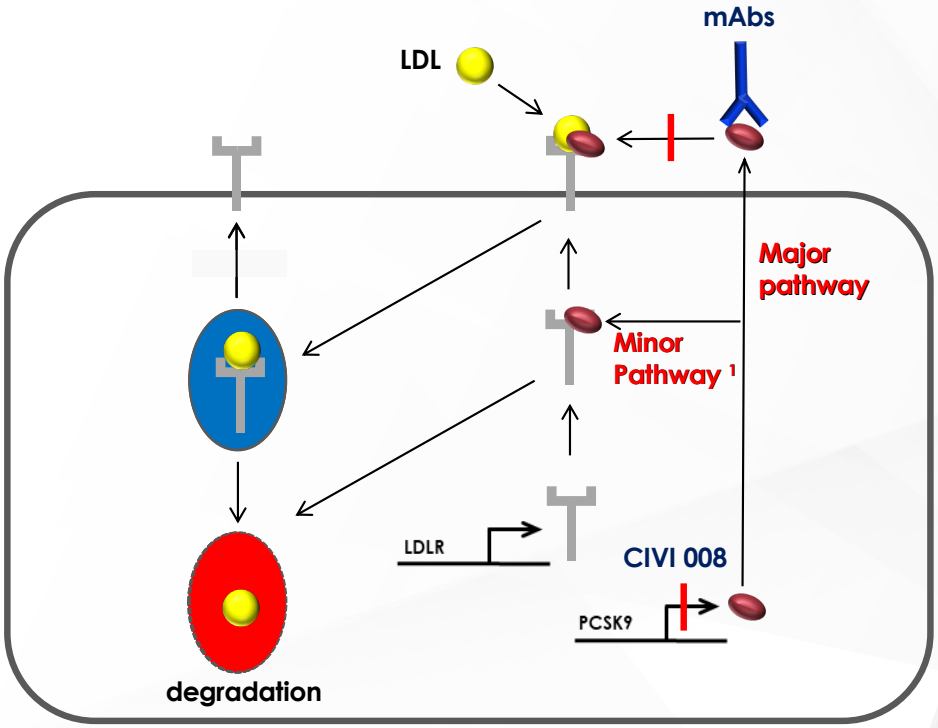
CARDIOVASCULAR DISEASE(CVD), PRINCIPALLY ISCHEMIC HEART DISEASE (IHD) AND STROKE, ARE THE LEADING CAUSE OF GLOBAL MORTALITY AND A MAJOR CONTRIBUTOR TO DISABILITY[1]

- Elevated LDL-C causes ASCVD and ranks (behind blood pressure and diet) high in modifiable risk factors that could substantially reduce CVD burden.[1]
- It is now widely accepted that 'lower LDL-C for longer is better ' is the optimal treatment goal for hypercholesterolemia. Not infrequently, optimal control cannot be obtained with statins alone, especially those at high and very high risk[2]
- PCSK9s have now been added to treatment guidelines to fulfill this need by providing unprecedented LDL-lowering. They have proven clinical benefit at therapeutic prevention of ASCVD.[3,4]
- However, high prices and inconvenient dosing regimens remain significant barriers to broad PCSK9 use.[5]

We believe CIVI 008 has the potential to drive widespread uptake by combining mAb-like LDL impact with oral dosing convenience and a lower cost

[1] Roth GA et al. J Am Coll Cardiol 2020
[2] Braunwald E European Heart J 2021
[3] Grundy S et al J Am Coll Cardiol 2019
[4] MACH F et al. Eur Heart J 2019
[5] Baum SJ et al Clinical Cardiol 2017

CIVI 008 MOA: COMPARISON TO APPROVED ANTI-PCSK9 mAbs



Based on results of preclinical studies

[1]Lagace Curr Opin Lipidol (2014) 25: 387-393
[2] Choi RE et al. Nature Rev Cardiol (2021) 18;701-711
[3] Krittanawong et al. Curr Problems Cardiol (2021); doi.org/10.1016/j.cpcardiol.2021.101043

CIVI 008: TARGET PROFILE FOR HIGH RISK ASCVD

CIVI 008 targets maintenance of the durable profile of mAbs with potentially greater convenience and cost-effective profile

	CIVI 008 (Target Product Profile)	mAbs	Inclisiran
LDL Reduction	Stable and robust LDL reduction of >60% throughout the steady-state dosing cycle	(~60% and stable through the dosing cycle)	~50% time averaged reduction with return towards pre-treatment level by end of dosing cycle
Safety Profile	Clean safety profile	Clean safety profile	Clean safety profile
Dose and route of administration	Daily Oral	Subcutaneous injection only: every two weeks or monthly by multiple injections or on-body infusion	Subcutaneous injection only: day 1, month 3 and every 6 months thereafter
COGS	Expected low	High	Higher

SIZEABLE POTENTIAL MARKET OPPORTUNITY FOR ORAL PCSK9 IN SECONDARY PATIENTS

Market Segmentation				Patients on Statin Not Achieving Target[1] (2031)	Target CiVi Oral Share[1]	Assumed CiVi Patients [4] (2031)	Assumed Price[4]	CiVi Market Size Opportunity
POPULATION WITH ELEVATED LDL-C[1] (35% of Adult Population in USA 250 Million in 2025)	NON-FAMILIAL (99%)	PRIMARY (42%)[3]	LOW RISK					
			HIGH RISK					
		SECONDARY (58%)[3]	LOW RISK LDL 70-100	5.8 Million	10%-15%	580K-870M	*$2k-$3k*	**$1.2B-$2.6B**
			HIGH RISK LDL>100	5.8 Million	25%-30%	1.45M-1.74M		**$2.9B-$5.2B**
	FAMILIAL[2] (both HeFH and HoFH)	ALL	ANY	112 k	35%	39 k		**$78M - $117M**
			Total	11.7 M	17%-22%	2.1M-2.6M	*$2k-$3k*	**$4.2B - $7.8B US**

1. 8.2 million on Statin * 70.5% of patients "not controlled" (Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association Emelia J. Benjamin et al., Circulation March 6, 2018, Volume 137, Issue 10) 2. Familial Hypercholestorilemia: Approx. 1 per 250 in adult U.S. population (based on NHANES; not genetically confirmed). Knowing the Prevalence of Familial Hypercholesterolemia Matters, Circulation 2016;133:1054-1057 http://circ.ahajournals.org/content/133/11/1054 3. CDC 2017 (NHANES, 2003-2014) 4. Internal modeling

COPE ASO Platform

Enabling oral delivery of oligonucleotide drugs currently administered subcutaneously allowing new convenient dosing of several product candidates with high potential commercial value

COPE PLATFORM OPPORTUNITY

Technology that enables safe and effective oral delivery is potentially the next frontier in oligonucleotide therapeutics. We believe such a technology has immense therapeutic potential

- In preclinical monkey studies, CIVI's proprietary COPE platform enabled oral delivery of different oligos and designs, supporting its broad utility for oral dosing of oligo therapeutics.
- The platform provides an opportunity for CIVI to:
  - Develop several product candidates within a relative short timeframe and at modest cost, and
  - Further monetize the platform beyond CIVI 008 through out-licensing to large pharma/biotech.
- IP broadly covering COPE platform filed world-wide in 2021.

CIVI 030

(IV Iloprost)

A potent vasodilator and platelet inhibitor with anti-inflammatory and anti-fibrotic effects in development for the treatment of frostbite

SEVERE FROSTBITE HAS SIGNIFICANT UNMET NEED AND OFFERS A UNIQUE COMMERCIAL OPPORTUNITY

- Intravenous iloprost is approved outside the US for several vascular conditions and is in the Wilderness Medical Society guidelines for the treatment of frostbite[1]
- Several published studies have documented a significant impact on amputation rates in frostbite patients
- Granted priority review with PDUFA July 18th
- Efficient commercialization strategy designed to optimize profitability with targeted R&D providing potential future upside

[1]McIntosh SE, et al. *Wilderness Environ Med.* 2019;30:S19-S32.

FROSTBITE REPRESENTS A SMALL POPULATION WITH SIGNIFICANT UNMET NEED DUE TO IRREVERSIBLE MORBIDITY

- US annual incidence of frostbite patients treated at hospitals estimated at ~14k[1]

  Grade 3 amputation rates 31% - 67% Grade 4 amputation rates > 95%

- Due to severity of injury and amputation risk, frostbite is expensive to treat with mean US hospital inpatient charges of ~$70k with readmissions >$200k[2,3] (data from 2018 and 2021)
- Cases include both urban frostbite and outdoor recreation frostbite
- Published data suggests amputation rate of >50% for severe cases[4,5,6]; iloprost has the potential to provide substantial risk reduction[5,6]
- Market research with P&T committee members was very positive with a clear appreciation of the potential value iloprost brings to reducing risk of amputation in frostbite

[1]Source: IQVIA Data; projected to account for estimated capture rate
[2]Nygaard RM, Endorf FW. J Burn Care Res. 2018;39:676-679. 2. [3]Endorf FW, Nygaard RM. J Burn Care Res. 2021;42:857-864.
[4]Cauchy E, et al. Wilderness Environ Med. 2001;12:248-255.
[5]Cauchy E, et al. N Engl J Med. 2011;364:189-190.
[6]Crooks S, et al. CJEM. 2022;24:622-629.