CiVi BIOPHARMA

Creating Novel Therapies to Treat Cardiovascular and Orphan Diseases

CORPORATE PRESENTATION

December 2020

Developing novel cardiovascular and metabolic treatments that bring meaningful therapeutic value to patients with unsatisfied medical needs in cardiovascular and/or rare diseases

INVESTMENT HIGHLIGHTS

- Pivotal Phase 3 clinical trial underway in Systemic Sclerosis (SSc), **an orphan disease with no FDA approved treatments**, representing a blockbuster market opportunity
- Robust pipeline of novel medicines addressing unmet needs in **cardiovascular and orphan diseases**
- Seasoned leadership team **with strong track record** in drug discovery, development and successful commercialization of therapies
- Supported by consortium of top U.S. and corporate VCs, led by **Boxer Capital, Roche Ventures, Tang Capital, RA Capital and a leading NYC-based biotechnology investment fund**

CLINICAL DEVELOPMENT PIPELINE

Robust clinical pipeline with mix of late-, mid- and earlier stage programs

Drug	Target	Rt of Admin	Indication	Development Stage				
				Pre-clin	Phase I	Phase II	Phase III	Commercial
Iloprost	IP-Rec.	I.V.	Systemic Sclerosis					
CIVI 007	PCSK-9	SubQ & Oral	Lipid disorders	SubQ ORAL				

EXPERIENCED MANAGEMENT TEAM

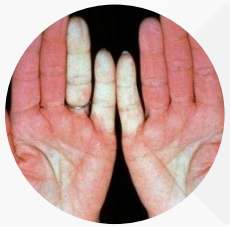
	**Shal Jacobovitz** **Chief Executive Officer**	• **30+ years experience in pharma industry leadership roles (Actelion U.S., F. Hoffman LaRoche, Abbott Canada, Nordic Labs & Marion Merrill Dow [now Aventis])** • **Former CEO of the American College of Cardiology (2013-2018)** • **Former President of 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 that discovered the CIVI 007 • 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** Vice President, Clinical Development	• 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 CEO of Eicos Sciences, Inc
	**Dinesh Khanna, MD, MSc** Medical Lead for Scleroderma Dev.	• Frederick G.L. Huetwell Professor of Medicine and Director, University of Michigan Scleroderma Program • Member of American College of Rheumatology and recipient of the Henry Kunkel Young Investigator Award. • Published over 350 peer-reviewed articles and book chapters
	**Kevin Christal** Vice President, Operations & Planning	•18 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.

CIVI 030

(IV Iloprost)

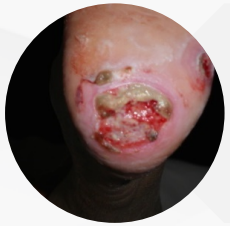
A potent vasodilator and platelet inhibitor with anti-inflammatory and anti-fibrotic effects in development for the treatment of Systemic Sclerosis (SSc)

DIGITAL ISCHEMIA IN SSC REPRESENTS A CONTINUUM THAT CAN PROGRESS FROM RAYNAUD'S PHENOMENON TO CRITICAL DIGITAL LOSS



Raynaud's Phenomenon; experienced by 95% SSc patients

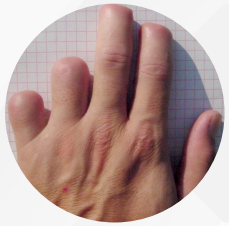
- SSc greatly exacerbates normal vasoconstrictive response to cold/stress
- Symptomatic attacks can be extremely painful and accompanied by numbness, tingling, and loss of dexterity



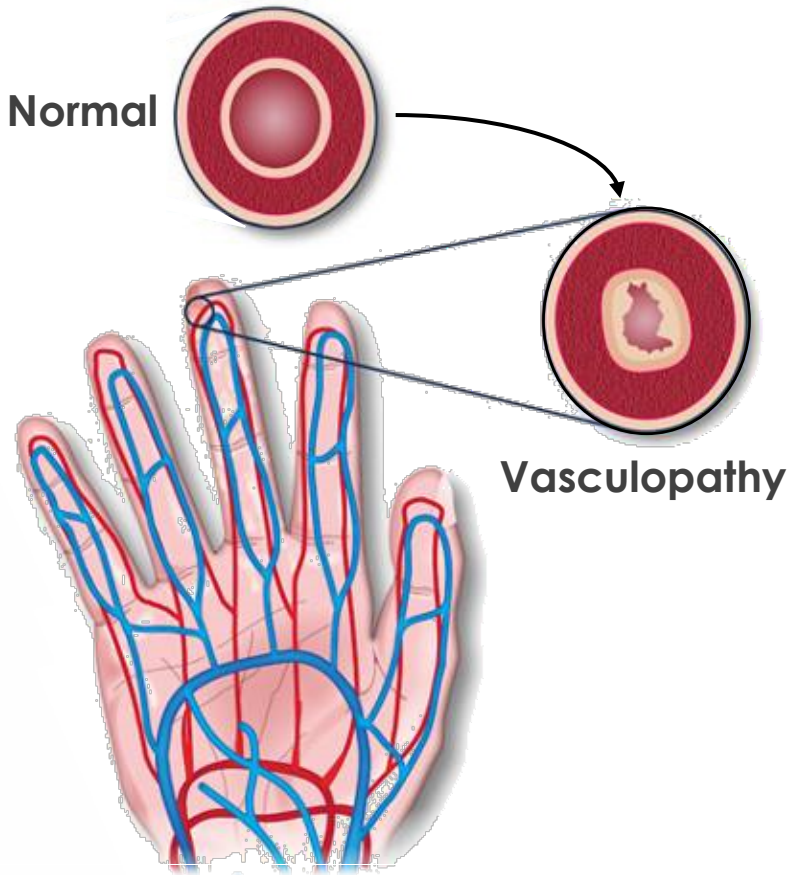
Digital Ulcers; 58% patients w/30% annual prevalence

- Necrotic lesions occurring at distal aspects of digits
- Can result in amputation, hospitalization, infection, gangrene

Gangrene in 10%, Infection in 26% over 2 years in patients with history of DUs (DUO Registry)[1]



Amputation in 16% over 2 years in patients with chronic DUs[1]



SSc results in digital ischemia due to progressive occlusive vasculopathy with compromised vessel lumen

[1]Matucci-Cerinic M, Krieg T, Guillevin, *et al. Ann Rheum Dis* 2016; 75:1770-1776.

SUBSTANTIAL CLINICAL DATA SUPPORTING EFFICACY AND SAFETY OF INTRAVENOUS ILOPROST IN SSC

Multiple studies over past 30 years demonstrating efficacy and safety of IV iloprost in SSc-related vasculopathy (Raynaud's and digital ulcer healing)

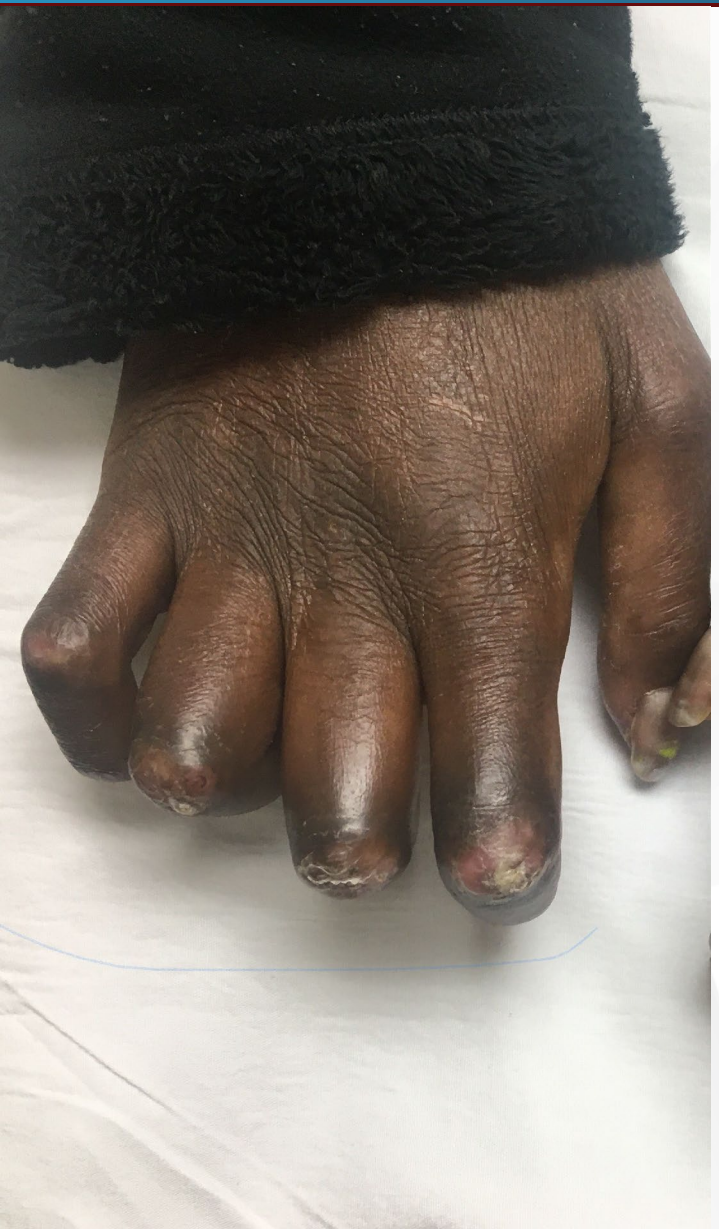
Most frequently administered as a 6-hour continuous infusion on 5 consecutive days with benefits lasting up to 9 weeks post infusion

EU approval for RP based primarily on DBPC study in SSc (n=131) demonstrating improvement in RP attack frequency vs placebo ($p<0.01$)

No FDA approved treatments for SSc-vasculopathy with SOC in US; primarily limited to lifestyle modifications and off-label oral vasodilators (CCB, PDE5)

Visalli E et al. *J Rare Dis Res Treat.* 2017;2:6-13. Wigley FM et al. *J Rheumatol.* 1992;19:1407-1414. Wigley FM et al. *Ann Intern Med.* 1994;120:199-206.

DIGITAL ISCHEMIA IN SSC HAS A SUBSTANTIAL IMPACT ON PATIENT QOL



If you can imagine a labor pain in your fingers, it's like in between it's fine, but when it's there it's like oh, my gosh, it really takes all your attention

Open ulcerations are the most miserable thing. The only thing I can compare it to is if you [have a] paper cut and pour lemon juice in it...For me, when my Raynaud's causes the open ulcerations that's a 24/7 issue for me

Think of everything you do with your hands and Raynaud's affects it

THE LARGEST DBPC[1] STUDY FOR IV ILOPROST IN SSC SHOWED A ROBUST TREATMENT EFFECT ON SSC-RP ATTACK FREQUENCY AND SEVERITY

Study	Design	N	Treatment Dose & Duration	Baseline weekly attack	RP Attack Frequency Results	RP Severity Score Results
Wigley et al, 1994	RCT [active-pbo parallel]	131	0.5-2.0 ng/kg/min 5 days	▪ 28 Active ▪ 27 Placebo	Percent reduction from Weeks 1 to 3 – 34% for iloprost (p=0.002) – 16% for placebo Percent reduction over Weeks 1 to 9 – 39% for iloprost (p=0.005) – 22% for placebo	Percent reduction from Weeks 1 to 3 – 31% for iloprost (p=0.006) – 13% for placebo Percent reduction over Weeks 1 to 9 – 35% for iloprost (p=0.01) – 20% for placebo

Intravenous Iloprost Infusion in Patients with Raynaud Phenomenon Secondary to Systemic Sclerosis: A Multicenter, Placebo-controlled, Double-Blind Study

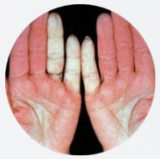
Fredrick M. Wigley, MD; Robert A. Wise, MD; James R. Seibold, MD; Deborah A. McCloskey, RN; Gregory Kujala, MD; Thomas A. Medsger, MD; Virginia D. Steen, MD; John Varga, MD; Sergio Jimenez, MD; Maureen Mayes, MD; Philip J. Clements, MD; Steven R. Weiner, MD; John Porter, MD; Michael Ellman, MD; Christopher Wise, MD; Lee D. Kaufman, MD; John Williams, MD; William Dole, MD

1 DBPC: Double-blind placebo controlled

PHASE 3 TRIAL IS UNDERWAY AT US SITES

AURORA

A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Phase 3 Study Evaluating the Safety and Efficacy of Intravenous Iloprost in Subjects With Systemic Sclerosis Experiencing Symptomatic Digital Ischemic Episodes



Primary Endpoint

Change of symptomatic digital ischemic episodes, as measured by weekly frequency of symptomatic Raynaud's attacks

Sites

~30 US sites

Sample

Up to n=180

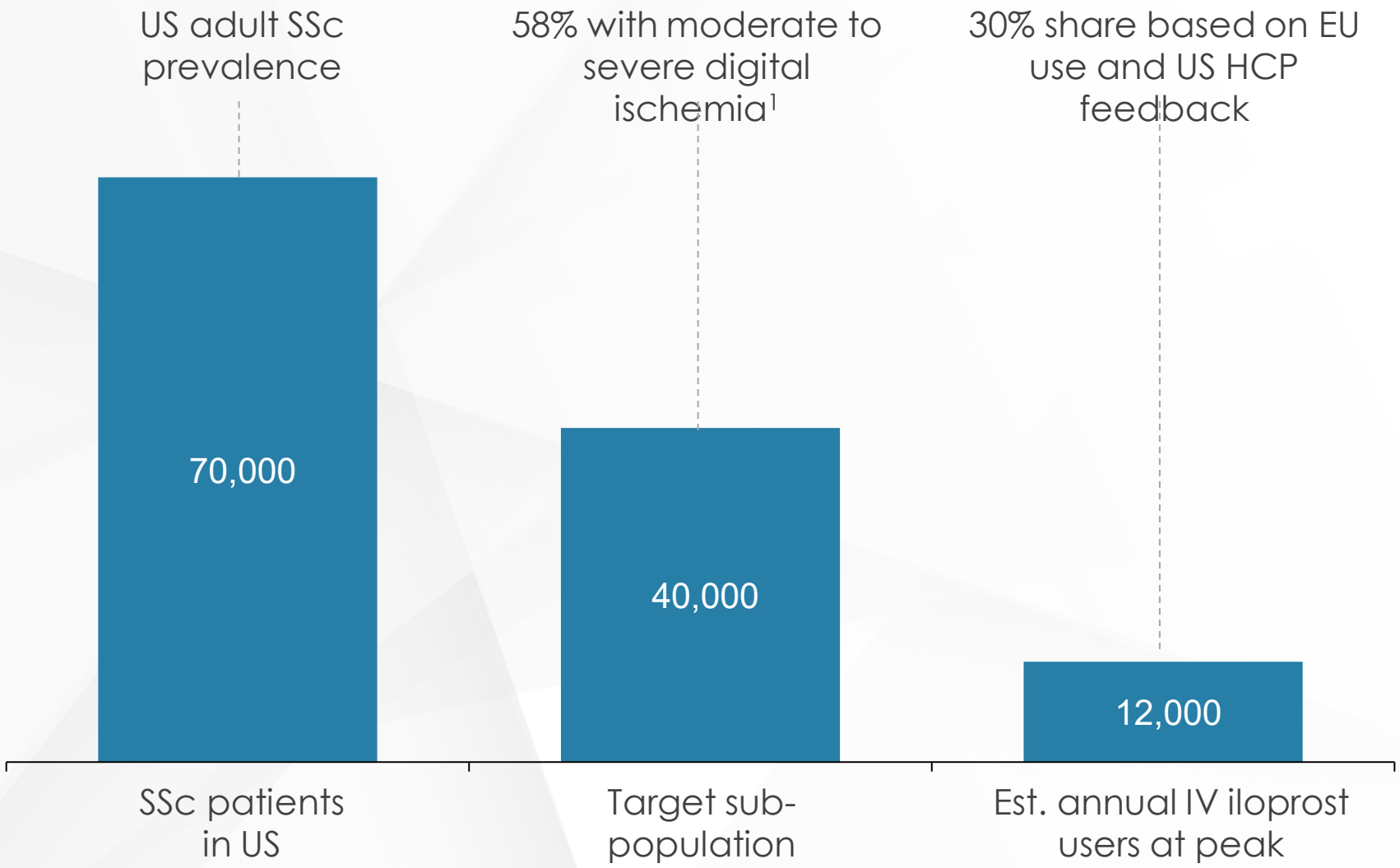
Topline Data

Mid-2021

Phase 2 Pilot

Completed Q3 2019

SIGNIFICANT REVENUE POTENTIAL WITH RAPID UPTAKE ANTICIPATED



1 Overall incidence of digital ulcers used as proxy to estimate proportion of patients with moderate to severe digital ischemia

Favorable initial pricing feedback with peak revenue opportunity ~$1B

FAVORABLE PRICING RANGE BASED ON INITIAL PAYER FEEDBACK AND ANALOGUES

Initial payer feedback suggests favorable pricing in-line with specialty rheumatology analogues

Administration profile will self-limit product to patients deriving significant benefit

Rheumatology Large Market

- RA, Psoriasis: JAK inhibitors, IL-23/17, TNFs
- ~$60k up to $90k

Prostacyclin class for PAH

- $200k+

Rheumatology specialty

- Nintedanib; SSc-ILD: $120k
- Pegloticase; gout: $200k+

MARKET DYNAMICS WILL ALLOW FOR EFFICIENT TARGETING AND RAPID UPTAKE AT LAUNCH

Concentrated network of centers treat a high proportion of SSc patients

Majority of key centers are participating in Phase 3 program

High level of enthusiasm and familiarity with IV iloprost among US KOLs

Very motivated patient population with limited treatment options

WITH A POSITIVE PHASE 3, COMMERCIAL LAUNCH ANTICIPATED 2022 WITH PRIORITY REVIEW

2021

AURORA Phase 3 LPFV

AURORA Topline Results

NDA Submission

2022

PDUFA with Priority Review

PDUFA with Standard Review

NDA submission via 505(b)(2) regulatory pathway using Ventavis (inhaled iloprost) and iloprost literature to support safety

FDA Orphan Drug Designation (ODD) for iloprost for the treatment of Systemic Sclerosis received May 2019

ODD provides 7 years market exclusivity from time of NDA approval

CIVI 007

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

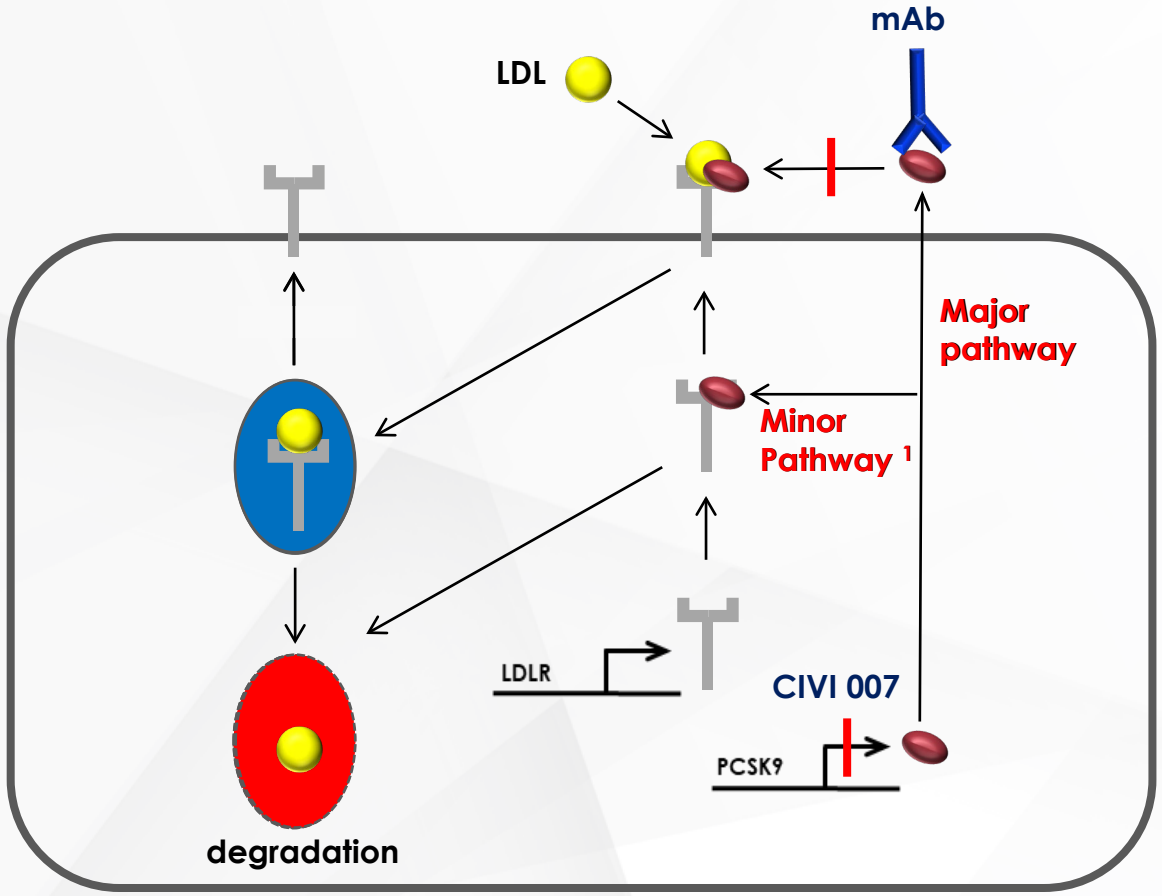
CVD REMAINS A LEADING CAUSE OF DEATH GLOBALLY[1]

- Elevated LDL-C causes ASCVD and statin therapy remains as SOC treatment.[2]
- Statin therapy will not always provide for optimal LDL levels (insufficient intensity, intolerance, non-compliance); estimates range from 36-80%.[3,4]
- PCSK9s (mAb's) provide unprecedented LDL-lowering, have proven clinical benefit and are poised to revolutionize therapeutic prevention of ASCVD.
- High prices and inconvenient dosing regimens remain significant barriers to broad PCSK9 use.

CIVI 007 has potential to combine mAb-like LDL efficacy with improved dosing convenience and a low cost of goods

[1] Heart Disease and Stroke Statistics—2019 Update. Circulation 2019; 139: e56-e528
[2] Lee et al JAMA Cardiol. 2016:1; 700-7
[3] Toth *et al.* Am J. Cardiovasc Drugs 2018 18: 157-173
[4] Ballantyne CM, et al. Am Heart J 2005;149:464-73.

CIVI 007 MOA: COMPARISON TO APPROVED ANTI-PCSK9 MAB'S



Major PCSK9 outcome studies demonstrate increased benefits of achieving LDL levels significantly below current treatment targets

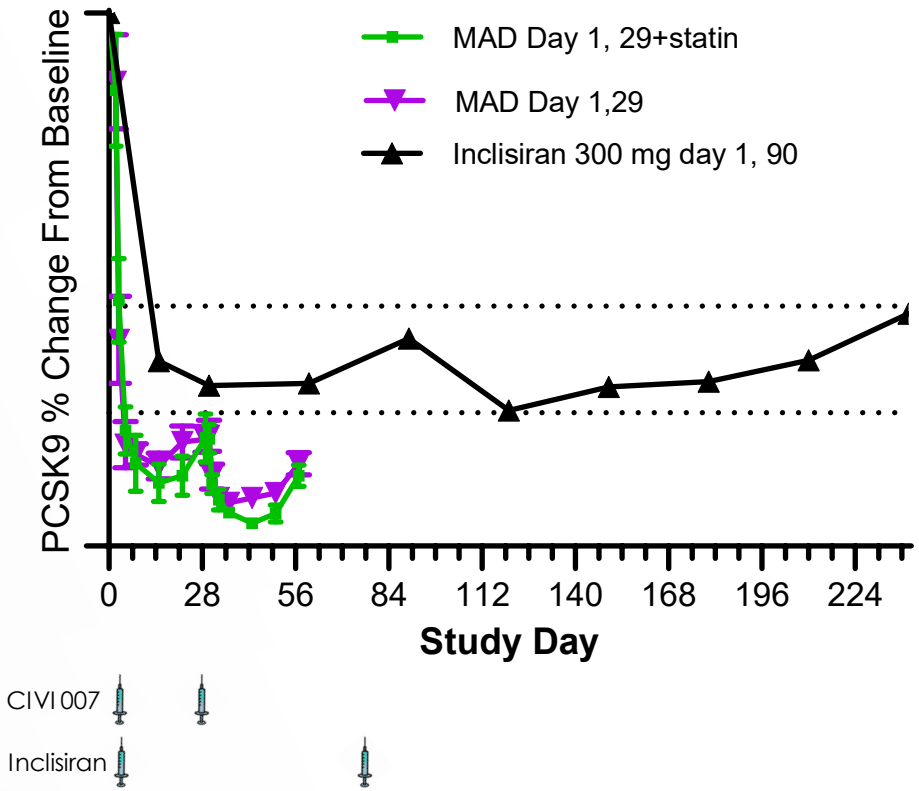
- Improved Lipid lowering compared to mAbs
- MoA more similarly mimics LoF mutations than mAb's , and may translate into improved outcomes
- Plasma ceramide profile (linked to reduced CV-risk[2]), more similar to human LoF than mAb profiles.
- Improved Lipid lowering in mAb non-responders due to mutations on PCSK9 binding site

[1] Lagace Curr Opin Lipidol (2014) 25: 387-393
[2] Data on specific serum markers for "ACS event survival" (Zora Biosciences) suggests that certain ceramides ar[1] Lagace Curr Opin Lipidol (2014) 25: 387-393
e highly predictive markers of outcome. Profiles from PCSK9 KO mice and human carriers of PCSK9-LoF are very similar and distinct from profiles in mAb treated patients.

CIVI 007: SC CLINICAL EXPERIENCE TO DATE

SAD/MAD study (36 subjects)

Expected pharmacologic profile associated with PCSK9 inhibition.



Source: CIVI 007; Phase 1 2 injection cohorts to day 57
Source: Orion-1 NEJM 2017; 376: 1430-40 (fig panel C)

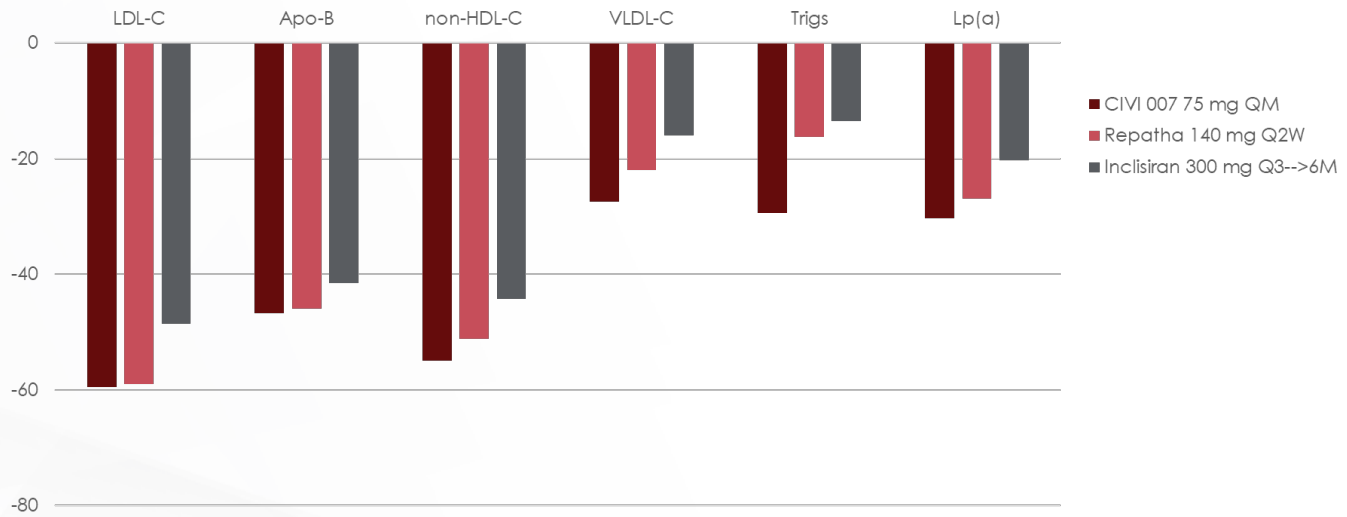
CIVI 007: SC EFFICACY SUMMARY

Expected pharmacologic profile associated with PCSK9 inhibition

Further work ongoing to define the optimal dose and route of administration for further clinical development

Phase 2a study: 37 actively-treated patients (interim data)

PERCENT CHANGE FROM BASELINE IN ATHEROGENIC LIPIDS AND LIPOPROTEINS



CIVI 007 data are Study 007-2-1 Day 43 mean changes from baseline (except VLDL-C and Trigs are median); combined 75 mf Q4W and 50→75 mg arms
Repatha data are from Fourier study; mean changes from baseline at 1 year except VLDL-C was not presented and data is from study -115 (statin combination study 140 mg Q2W at 12 weeks)
Inclisiran data are averaged from the Orion 10 and 11 trials reported time-averaged mean changes from baseline to day 90-540 of treatment

CIVI 007: BRIEF DEVELOPMENT STATUS

Work Completed To Date To Enable Development Progression

Proof-of-concept in NHPs

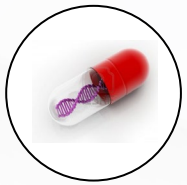
IND enabling, and chronic toxicity studies in rodents in SC and oral, and monkeys in SC

Phase I SAD/MAD (36 subjects)

Phase 2a (49 subjects)

Manufacture (kg scale) for phase 2

Work in Progress



Oral dosing in NHPs

CIVI 007: TARGET PROFILE FOR HIGH RISK ASCVD

CIVI 007 targets maintenance of the durable efficacy of MABs with a more convenient and cost-effective profile

CIVI 007 Target Product Profile	mAbs	inclisiran
Stable and robust LDL reduction of >60% throughout the dosing cycle	✓ (~60% and stable through the dosing cycle)	~50% time averaged reduction with return towards pre-treatment level by end of dosing cycle
Well tolerated and acceptable safety profile	✓	✓
Dose and route of administration: oral dosing under evaluation to optimize overall profile	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
Best-in-class COGS provide flexibility for competitive commercial positioning and solid business case outside the US	X	X

SIZEABLE MARKET OPPORTUNITY FOR ORAL PCSK9 IN SECONDARY PATIENTS

Market Segmentation				Patients on Statin Not Achieving Target[1] (2031)	CiVi Oral Share[1]	CiVi Patients (2031)	Price	CiVi Market Size
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					
		SECOND-ARY (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 Thou.	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)

CORPORATE & FINANCIAL SNAPSHOT

- Private company founded in 2017
- Offices in Washington, DC and San Francisco; 15 FTEs
- Orphan Drug exclusivity for lead product, CIVI 030
- CIVI 007 has long-lived composition of matter patents worldwide (2034)
- Leading venture and corporate investors (Leading NYC-based biotechnology investment fund, Boxer Capital, Roche Ventures, RA Capital and Tang Capital)
- Raised ~$120 million to date

UPCOMING MILESTONES

- Complete oral formulation of CIVI-007
- Complete enrollment of Phase 3 study of CIVI-030 in SSc
- Complete NHP, toxicology and initiate Phase 1/2 studies of oral CIVI 007
- Complete manufacturing of registration batches for CIVI 030
- Topline data readout from CIVI 030 Phase 3 AURORA study
- NDA Submission of CIVI 030 as a treatment for SSc

www.civibio.com

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