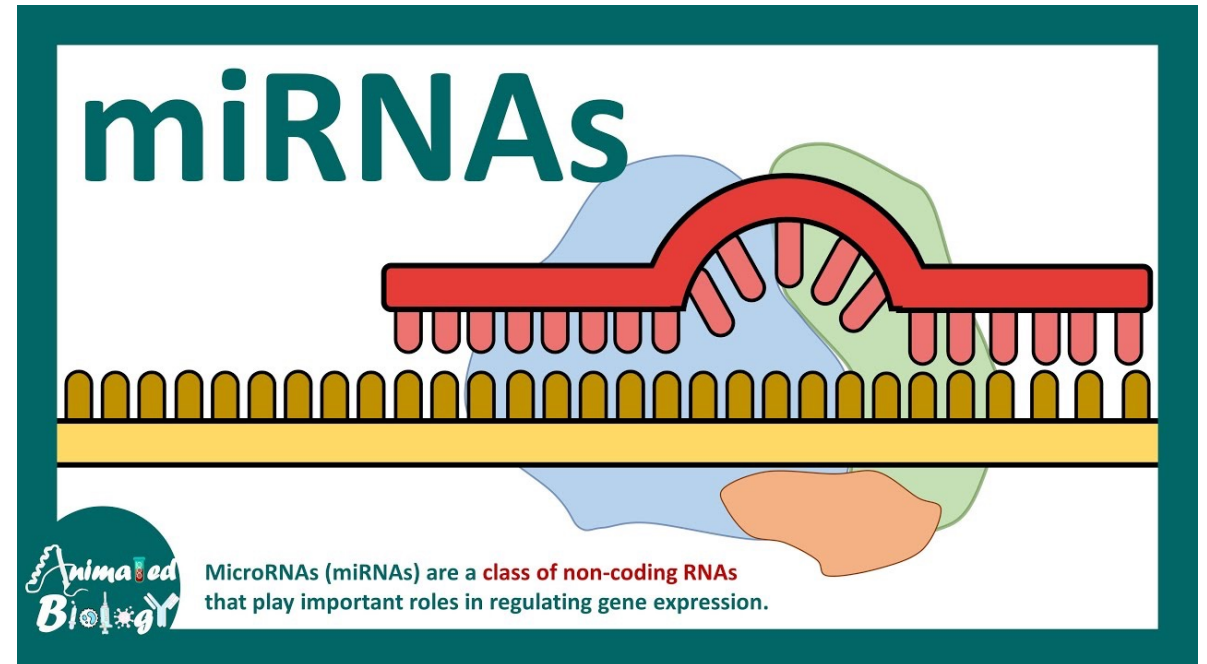




Mike Behr
CEO
C: 610-656-5229
E: mbehr@prolifagen

Regenerating Damaged Heart Muscle with Micro-RNA Technology



Executive Summary

PROBLEM

Damaged Heart Muscle Does Not Regenerate.

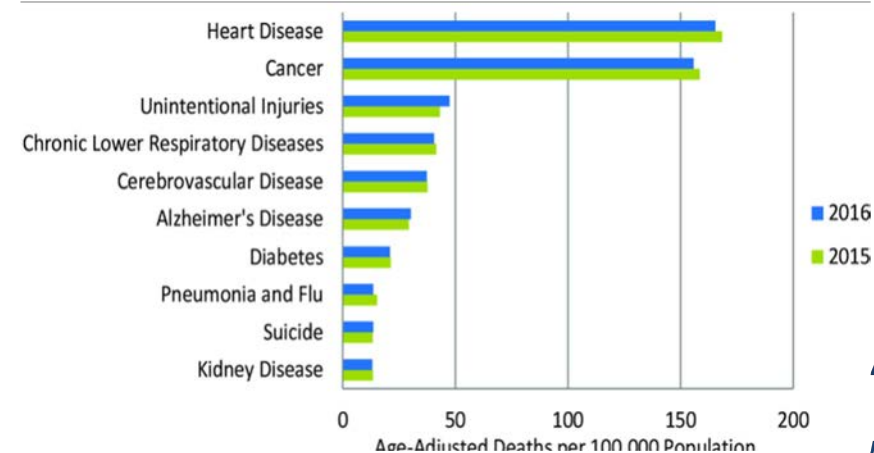
- 800,000 Heart Attacks in the US annually.
- #1 Cause of Death in US & Globally
- Increase Risk of Repeat MI and progression to Heart Failure.



SOLUTION

Delivery of miRNA302 to Damaged Heart Muscle.

- PRO302 proprietary mix delivered transiently to the affected area.
 - miRNA 302
 - Hydrogel



Value Proposition / Return on Investment

Novo Nordisk Acquires Cardior Pharmaceuticals for \$1.112B in Effort to Bolster Cardiovascular Disease Pipeline

March 26, 2024
By Don Tracy, Associate Editor

News Article



Deal includes the novel treatment CDR132L, which is currently in Phase II clinical trials for heart failure.

Novo Nordisk announced that it has acquired Cardior Pharmaceuticals in hopes of improving its pipeline in cardiovascular disease management. The acquisition includes Cardior's top drug candidate, CDR132L, which is currently in Phase II of clinical development



Image Credit: Adobe Stock Images/ckybe



\$1.1B



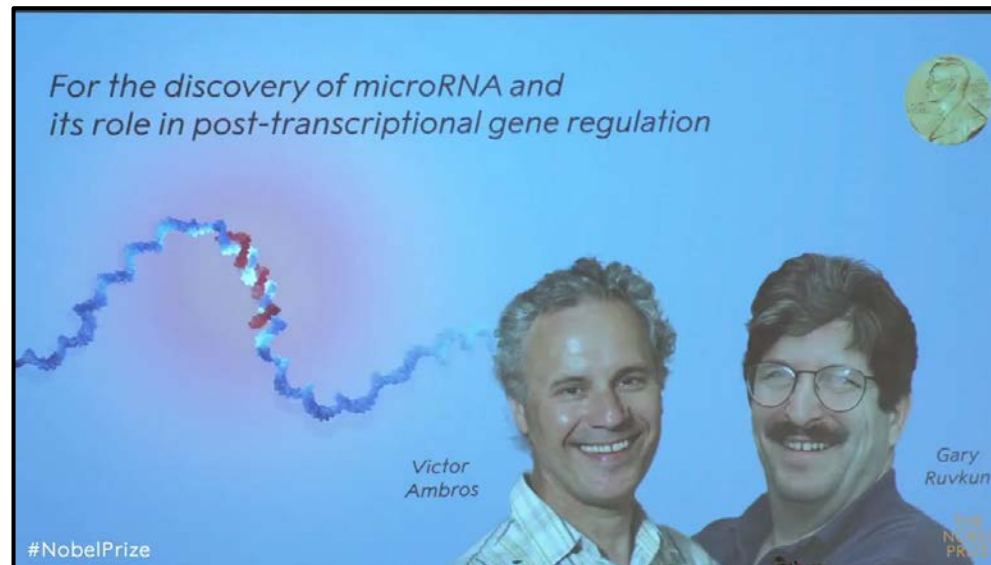
Novartis to acquire Regulus Therapeutics and farabursen, an investigational microRNA inhibitor to treat ADPKD, the most common genetic cause of renal failure

Apr 30, 2025

- Regulus is a clinical-stage biopharmaceutical company developing microRNA therapeutics with a focus on autosomal dominant polycystic kidney disease (ADPKD), a severe renal disease
- Lead asset for ADPKD, farabursen, is a novel, next-generation oligonucleotide targeting miR-17 that recently completed a Phase 1b multiple-ascending dose clinical trial
- Transaction includes USD 0.8 billion upfront with a potential additional USD 0.9 billion payment upon the achievement of a future regulatory milestone; transaction is expected to close in the second half of 2025, subject to customary closing conditions



\$1.7B



Team: Leadership & BOD



Mike Behr
CEO-BOD

- 30+ Years in Life Science Industry
- Multiple Ground-Up Start Ups
- Successful Exit & No Liquidations



Kiernan Seth, PhD
CDO

- 25+ Years in BioPharma Industry
- Lexicon, Pfizer, BMS
- Cardiovascular Electrophysiology



Andreas Bader, PhD
Consulting CSO

- 20 Years Biotech R&D
- Phase I & II Clinical Trials
- Multiple Start-Up Exits
- Co-Founder of Mirna: 1st miR Clinicals



Will Houston, CFA
CFO

- CFO to Multiple LS Start-Ups
- Financial Model Strategies
- 20+ years Life Science Ventures



Claudine Bruck, PhD
BOD-Founder
30 Years GSK
Multiple BOD Seats



Alex Shaw, PhD
BOD
Multiple LS Start-Ups
Multiple Exits



Dave Pfeiffer, MBA
BOD
Multiple Life Science CEO
Multiple BOD Seats



OPEN
BOD

Team: SAB & Consultants



Ed Morrissey, PhD
Scientific Founder
SAB Chair
Univ of PA



Jason Burdick, PhD
Univ of Colorado



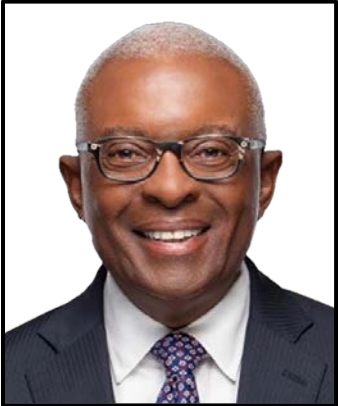
Gordana Novakovic, PhD
Columbia University



Jose Oberholzer, MD
Univ of Illinois
Zurich Univ Hospital



Leo Wang, MD, PhD
Univ of PA



Errol Taylor, JD
IP Consultant



Howard Herrmann, MD
Univ of PA



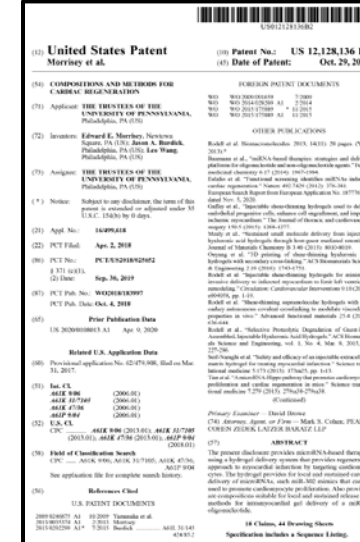
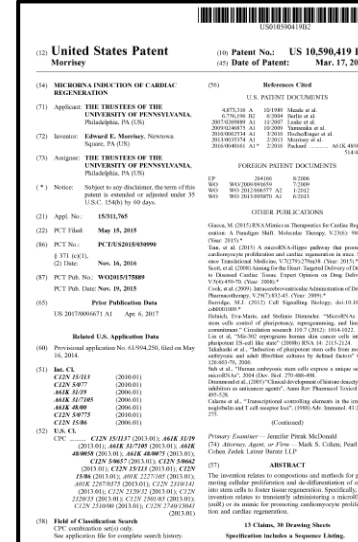
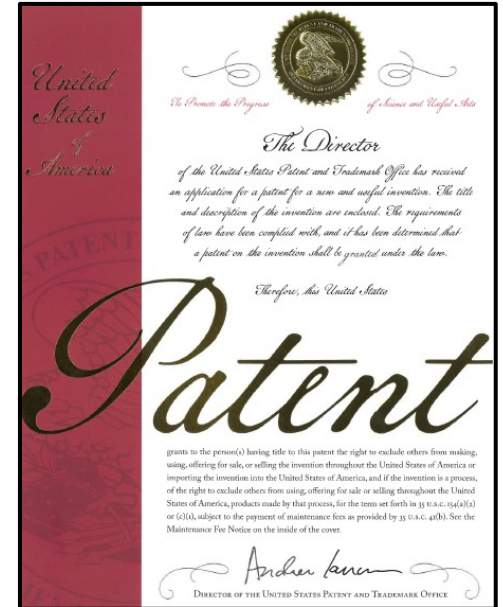
Rob Gorman, MD
Majoro Cardiac
Innovations

Prolifagen Intellectual Property

- US Patent 9,115,345
 - "Micro RNA Induction of Pluripotential Stem Cells"
 - Issue Date: 8/25/2015
 - Priority Date: 3/25/2011
- US Patent 10,590,419
 - "Micro RNA Induction of Cardiac Regeneration"
 - Issue Date: 3/17/2020
 - Priority Date: 5/15/2015
- US Patent 12,128,136
 - "Compositions of Methods for Cardiac Regeneration"
 - Issue Date: 10/29/2024
 - Priority Date: 4/2/2018

University of Pennsylvania

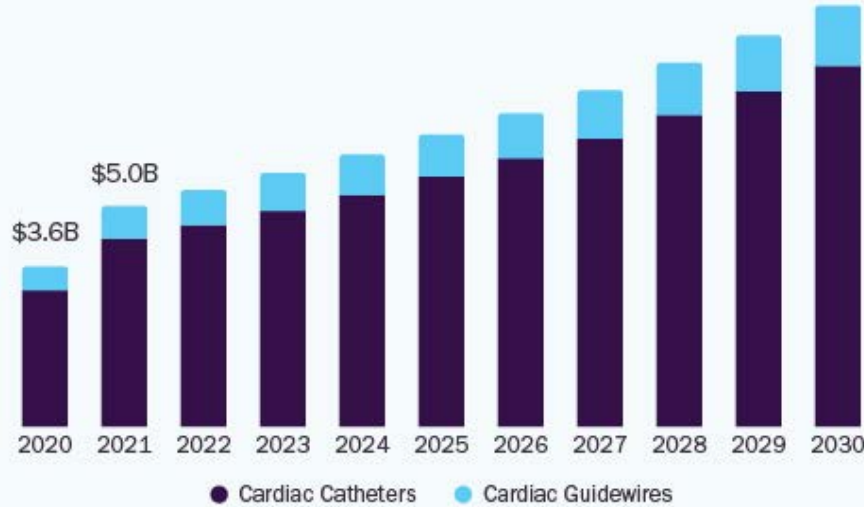
- Favorable Licensing Terms
- Exclusive License



Market

U.S. Cardiac Catheters & Guidewires Market

Size, by Product, 2020 - 2030 (USD Billion)



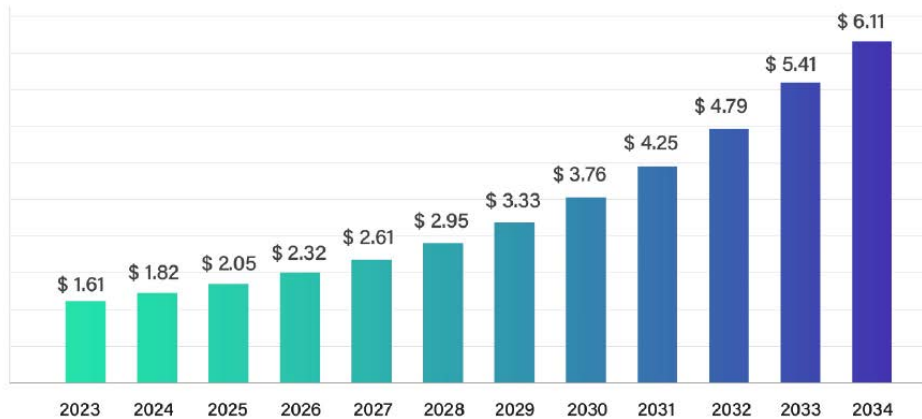
7.5%

U.S. Market CAGR,
2023 - 2030

Source:
www.grandviewresearch.com



microRNA Market Revenue 2023 to 2034 (USD Billion)



Source: www.towardshealthcare.com



11.8%

U.S. Market CAGR,
2024 - 2030

Source:
www.grandviewresearch.com



About

805,000

Americans suffer a heart attack
every year.

NOTE For 805,000 of them, it's their first heart attack.

SOURCE American Heart Association and the National Forum
for Heart Disease & Stroke Prevention

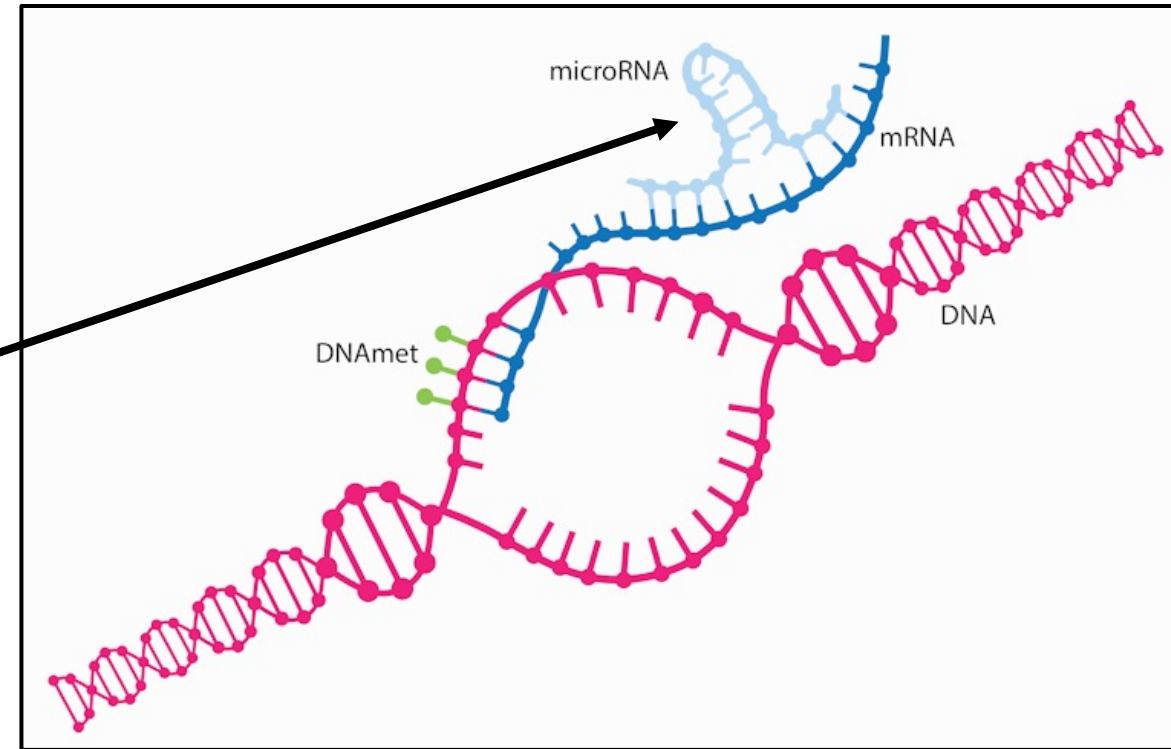
USA TODAY

Competitive Landscape

	Prolifagen miR-302	Gene therapy	Stem cells	Angiogenesis- focused approaches	Bio materials	Reperfusion injury prevention
Transient regeneration mechanism – safety	✓	✗	✗	✓	NA	NA
Timing: Opportunity for intervention outside of emergency situation	✓	✓	✓	✓	✓	✗
Single molecular entity (vs. gene therapy or exogenous cells)	✓	✗	✗	✓	NA	✓
Direct regeneration of <i>functional cardiac muscle</i>	✓	✓	✓	✗	✗	NA

What is micro-RNA (miR)?

- **DNA**
 - Carries information needed to build protein
- **mRNA**
 - Carries information from DNA
 - Template for Protein Production
 - Hundreds of Thousands of Nucleotides
- **siRNA**
 - Double Stranded / Exogenous
 - 19-23 Nucleotides
 - Regulate Gene Expression
- **miRNA**
 - Single Stranded / Endogenous
 - 22-23 Nucleotides
 - Regulate Cellular Processes



Prolifagen Technology: PRO302

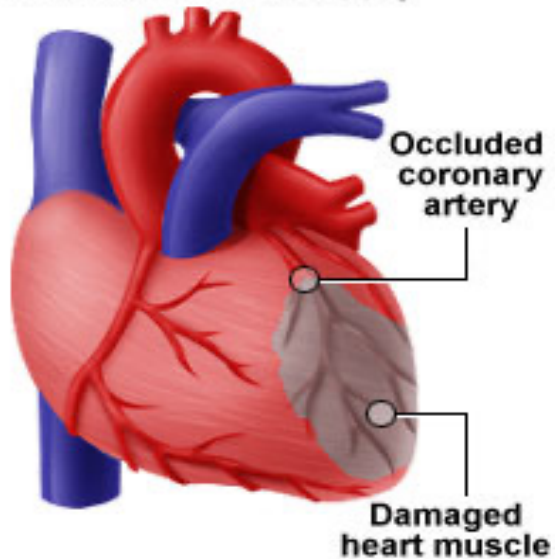
miRNA302

- Synthetic
- Controllable
- Switch on and then Switch Off

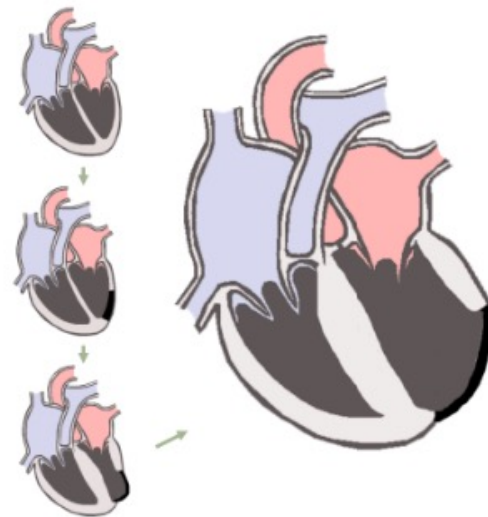
Hydrogel

- Hyaluronic Acid
- Shear Thinning
- Local & Transient

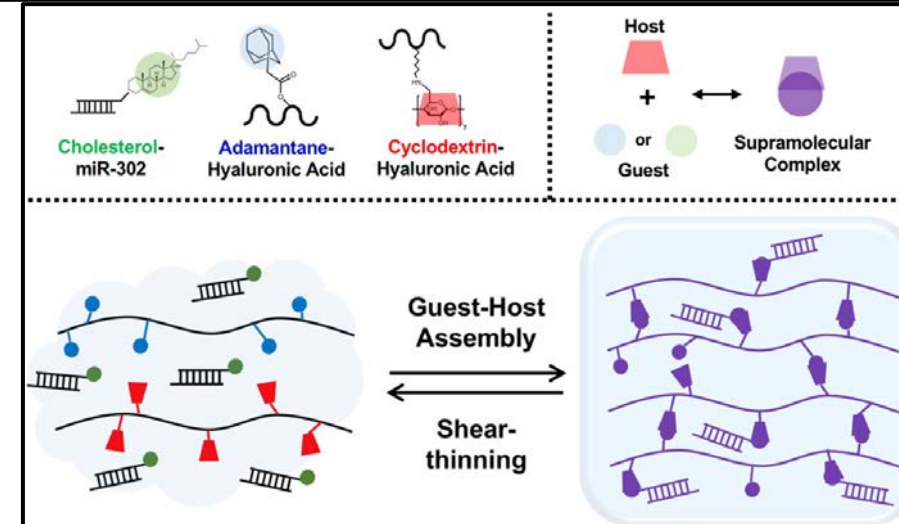
Blocked blood supply



Myocardial Infarction and Heart Failure



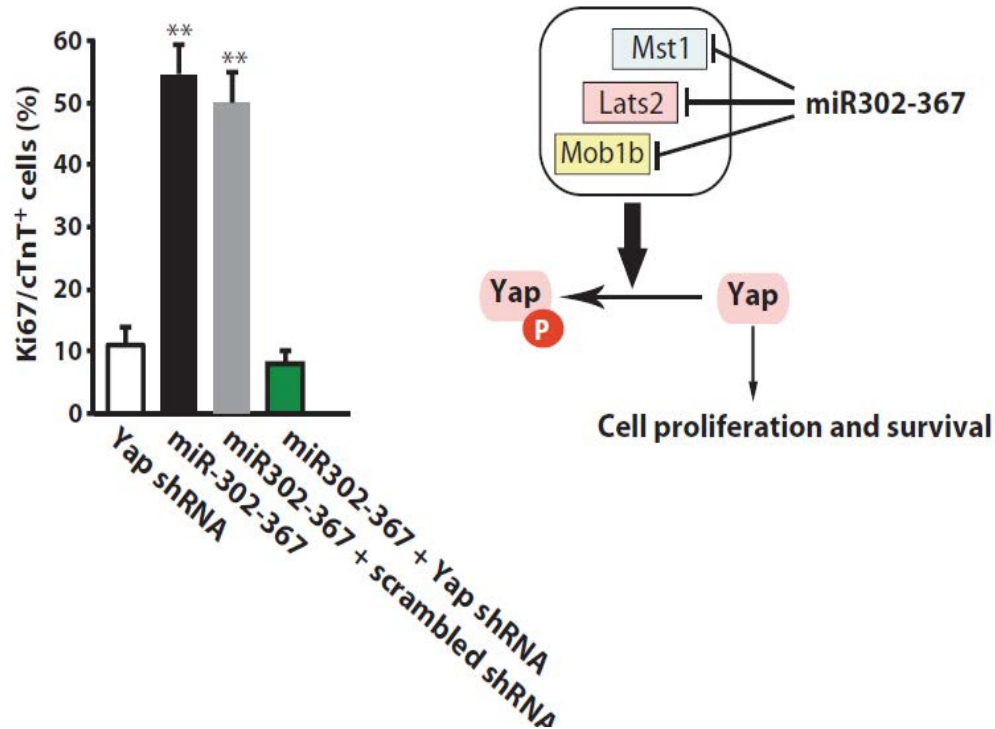
Myocardial Infarction
↓
Death of cardiomyocytes
↓
Scar tissue formation
↓
Thinning of the heart wall
↓
Left ventricular remodeling
↓
Decreased pumping capacity



Mechanism of Action

Hippo Pathway

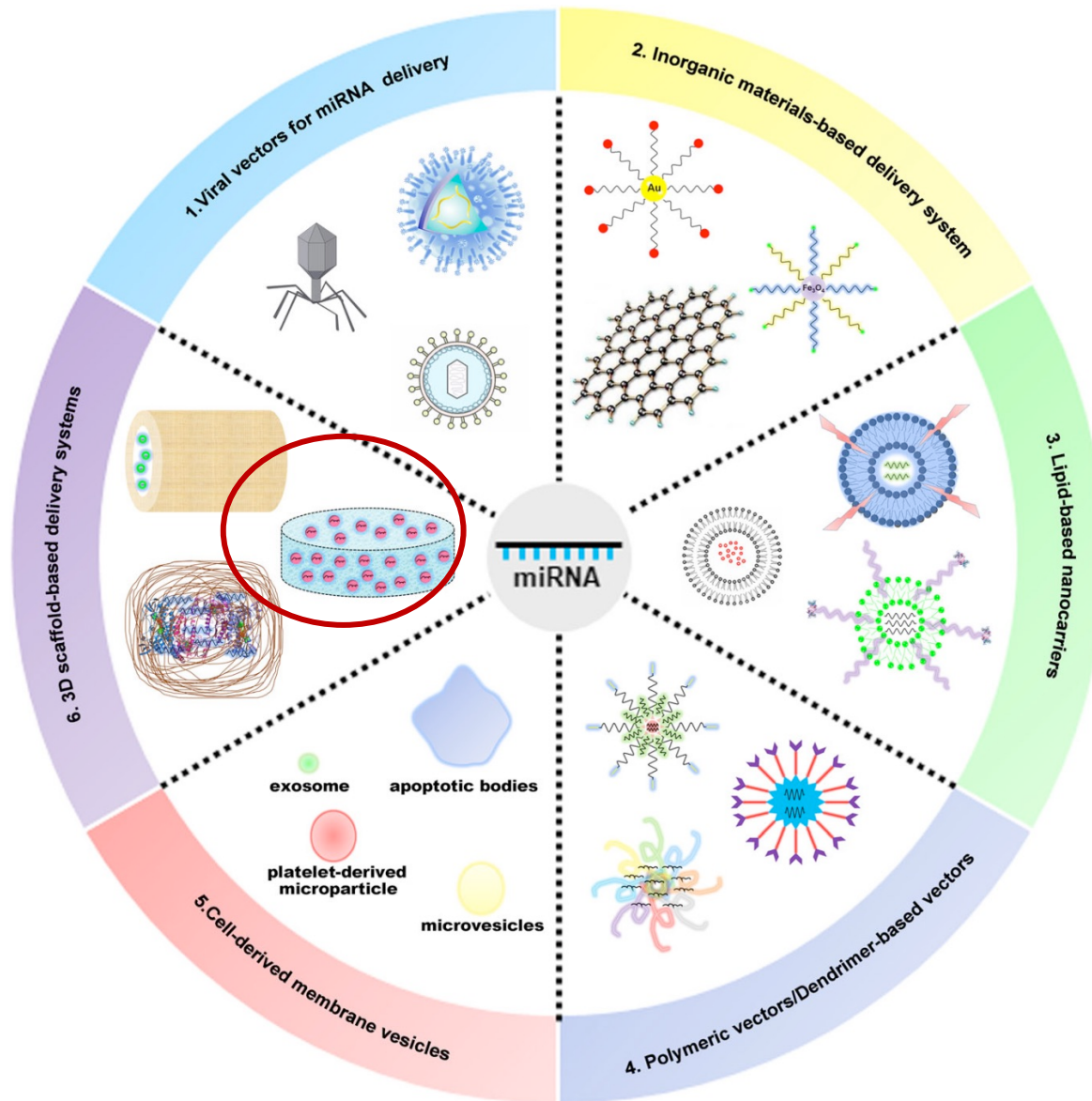
Supporting Literature



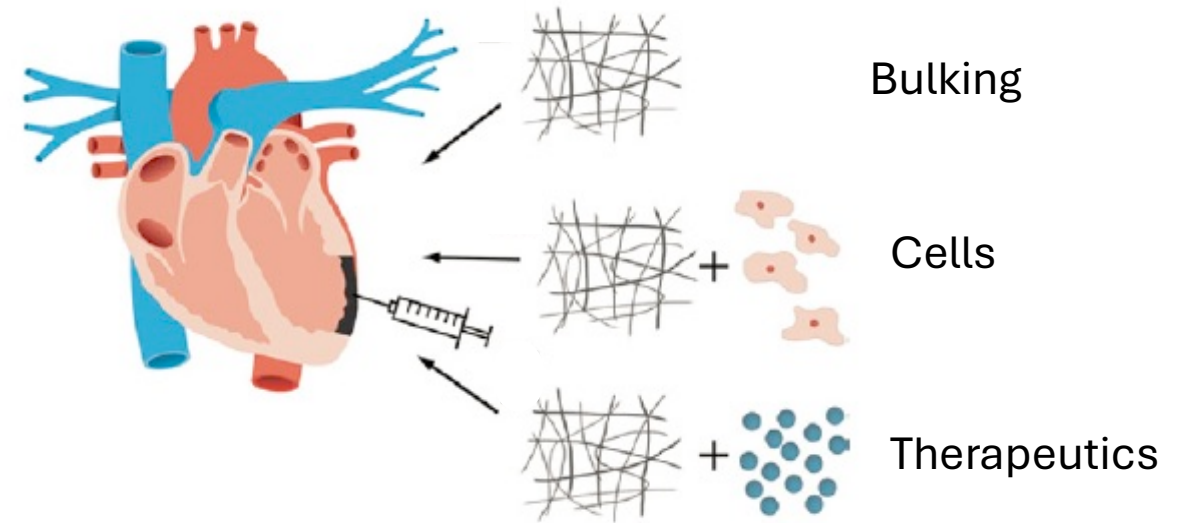
Hippo Pathway Deficiency Reverses Systolic Heart Failure Post-Infarction. Leach JP, Heallen T, Zhang M, Rahmani M, Morikawa Y, Hill MC, Segura A, Willerson JT, Martin JF, *Nature*. 2017; 550(7675): 260–264.

YAP Partially Reprograms Chromatin Accessibility to Directly Induce Adult Cardiogenesis In Vivo. Monroe TO, Hill MC, Morikawa Y, Leach JP, Heallen T, Cao S, Krijger PHL, de Laat W, Wehrens XHT, Rodney GG, Martin JF, *Dev Cell*. 2019; 48(6):765-779.e7.

miRNA Delivery Approaches



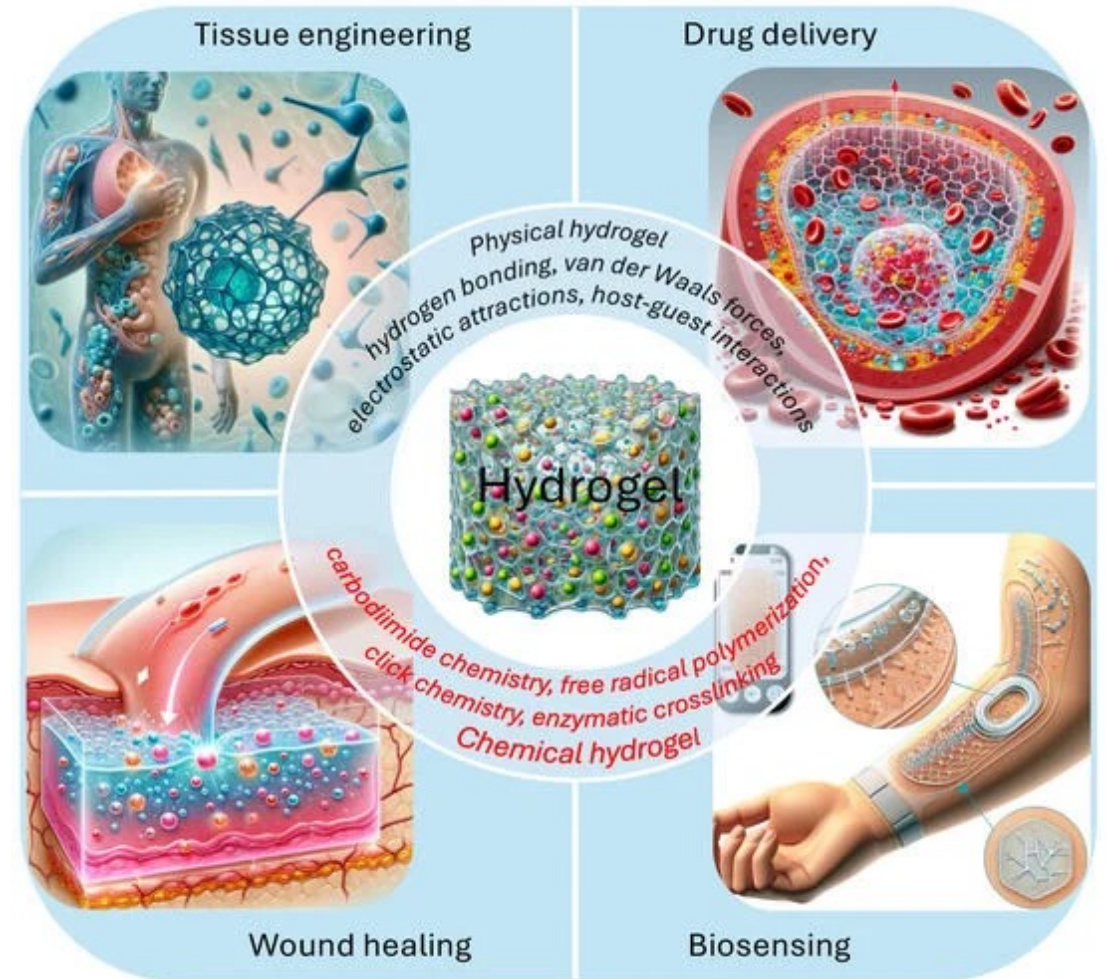
Hydrogels in cardiac repair



Rane, A. A. et al. *J. Am. Coll. Cardiol.* **2011**.

Hydrogel Delivery

- Composition
- In vitro sustained release work
- In vivo pharmacology data including
 - PK, CM proliferation (confetti) and functional effect
- Conditions for preserving RNA and hydrogel
 - Freezing
 - Lyophilization



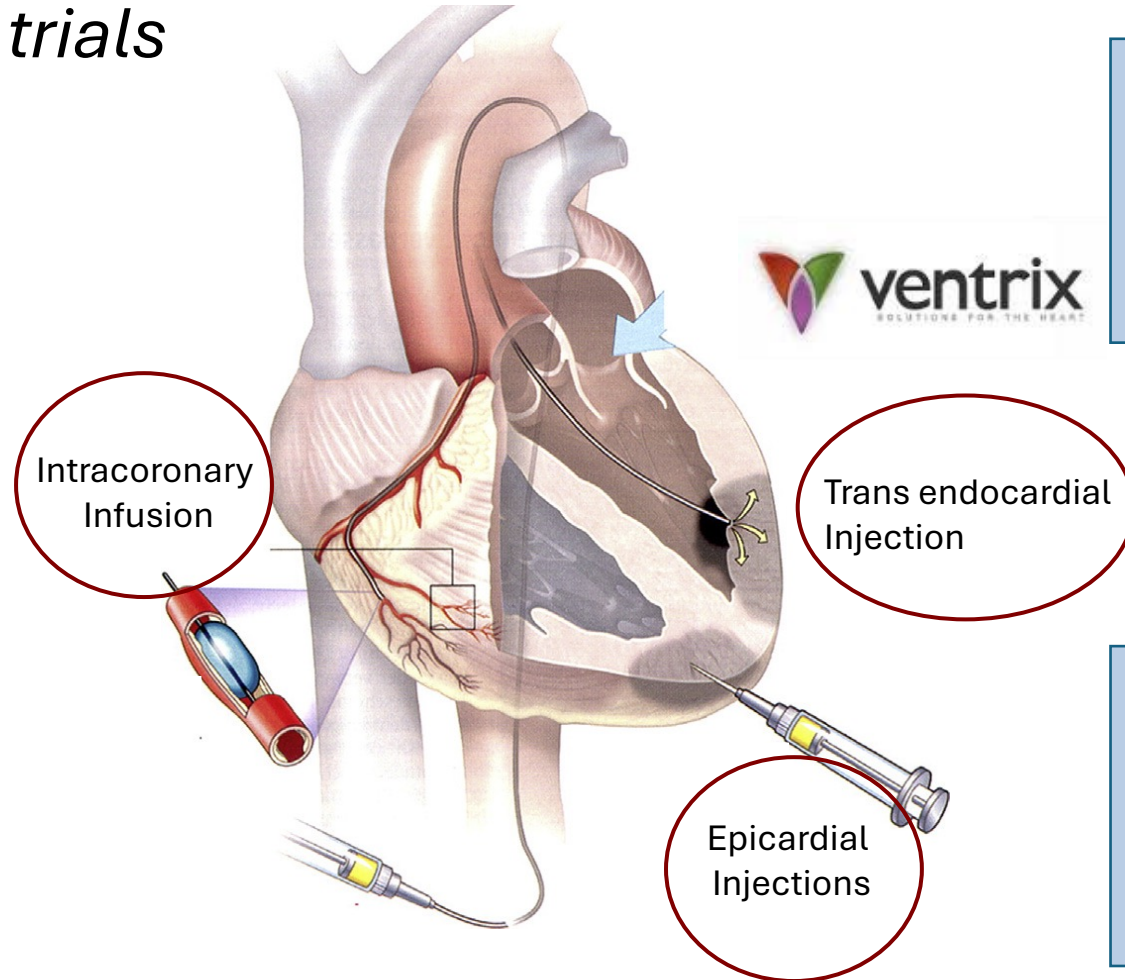
Hydrogels in Cardiac Repair

Hydrogels in clinical trials



Phase II: NCT01226563 (PRESERVATION I)

Large MI patients (303),
Safe, but not effective
*Too little material that actually
reaches infarct?*



Phase I: NCT02305602
60 days to 3 years after MI
(15)
MyoStar catheter
Safety shown

Phase II: NCT01311791 (AUGMENT-HF)

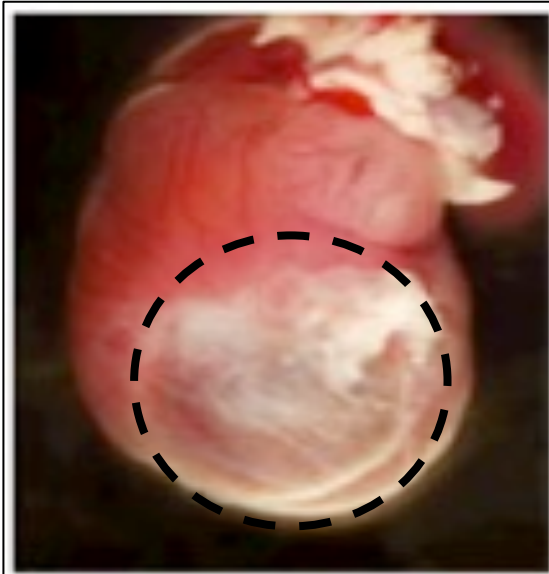
Heart failure patients (78)
Improved VO_2 levels,
No functional/remodeling changes
Delivered too late?



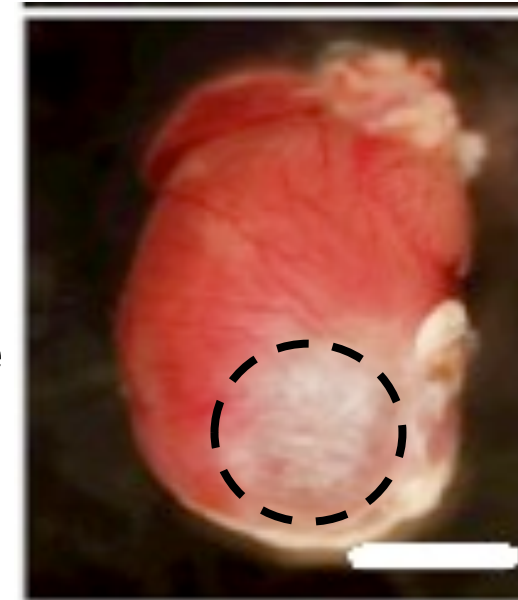
Proof of Concept

Pre-Clinical Data

- Mice Study
- In-Vitro Human Data
- Limited Pig Study

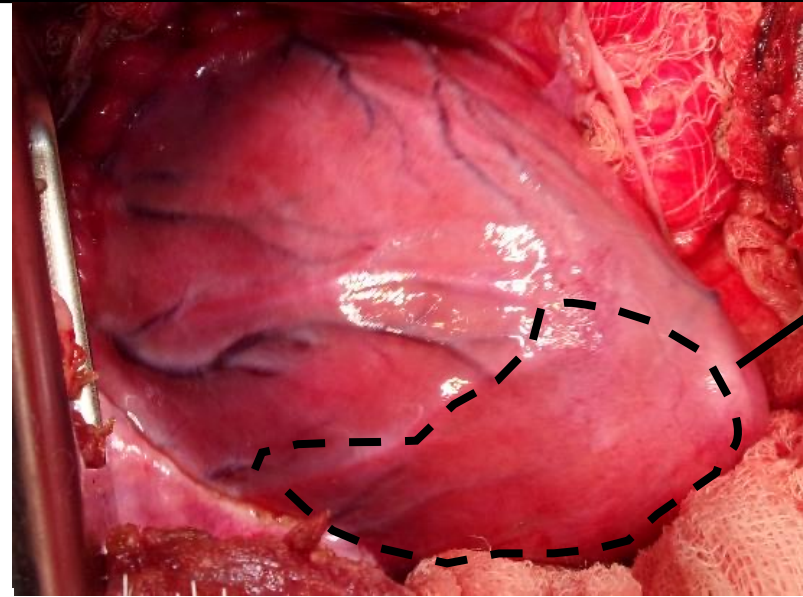
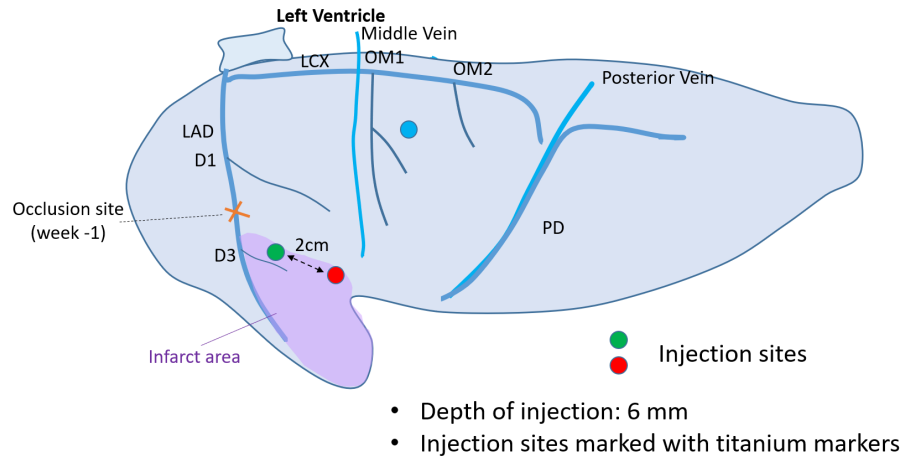


Mouse heart after heart attack treated with PRO-302 shows a reduced area of damaged tissue



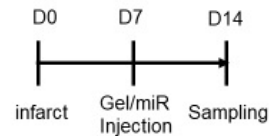
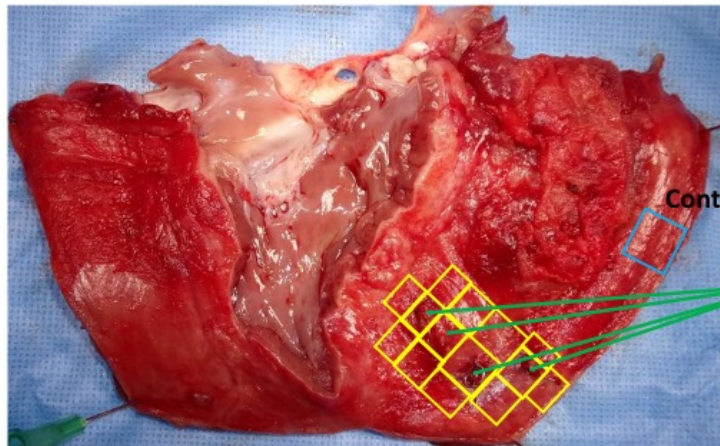
Initial Pig Study

Injection Diagram



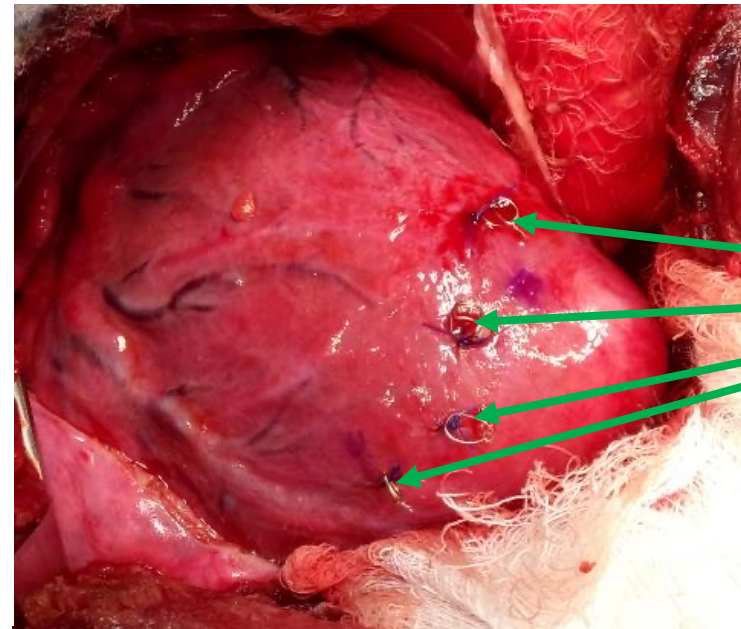
Infarct area

Pig Sampling Map



Control (healthy area)

4 Injection sites
Gel/miR-302
Marked with titanium markers



Marker for miR

- 14 tissue blocks around Gel/miR-302 injection sites were cut out.
- Tissue blocks were further cut horizontally into two or three pieces depending on their thickness
- A small section of each piece was snap frozen, and the rest was stored in 4% paraformaldehyde

Pig Study Results

Pharmacology dose-response in pigs

- PD marker: Cardiomyocyte proliferation at week 1
- Parameters tested:
 - Time of administration (1 week vs. 1 month after infarct)
 - Impact of injury zone (Infarcted vs. healthy)
- Proliferating Cardiomyocytes are observed in infarcted/PRO-302 injected zones, but NOT in healthy non-injected zones
- Strong proliferation of CM at 1-week, but NOT at 1-month

Heart Attack vs Heart Failure

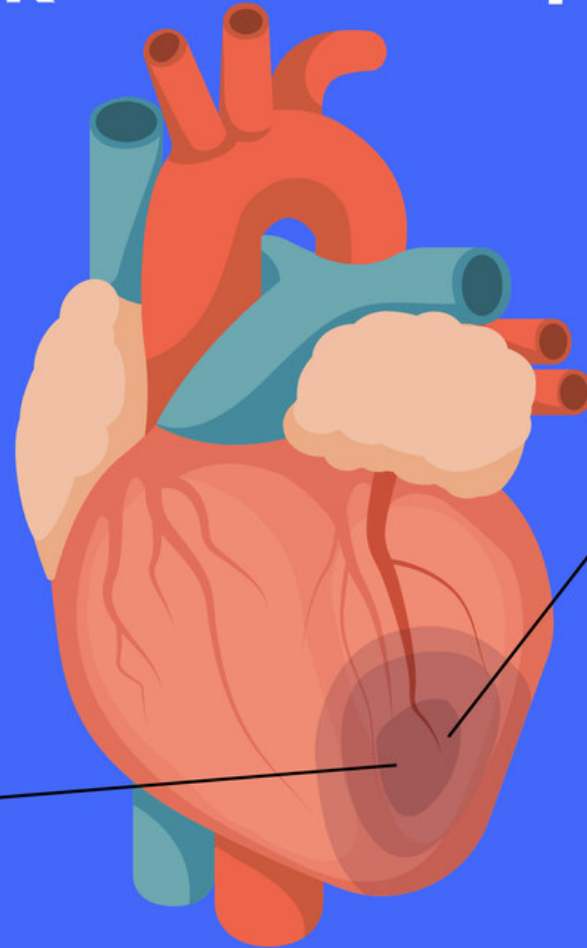
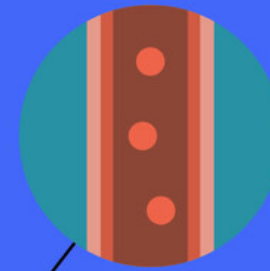
Heart Attack

Blood flow to the heart gets cut off due to coronary artery blockage



Heart Failure

Chronic, progressive disease in which the heart can't pump enough blood

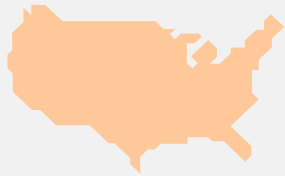


20-30% of Heart Attacks lead to Heart Failure

Heart Failure: #1 Cause of Hospitalizations for Americans 65+

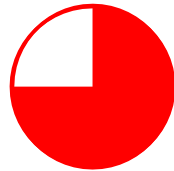
1,000,000

Hospitalizations for heart failure annually in the US



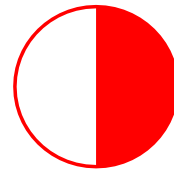
6.2M

in the US have heart failure



27%

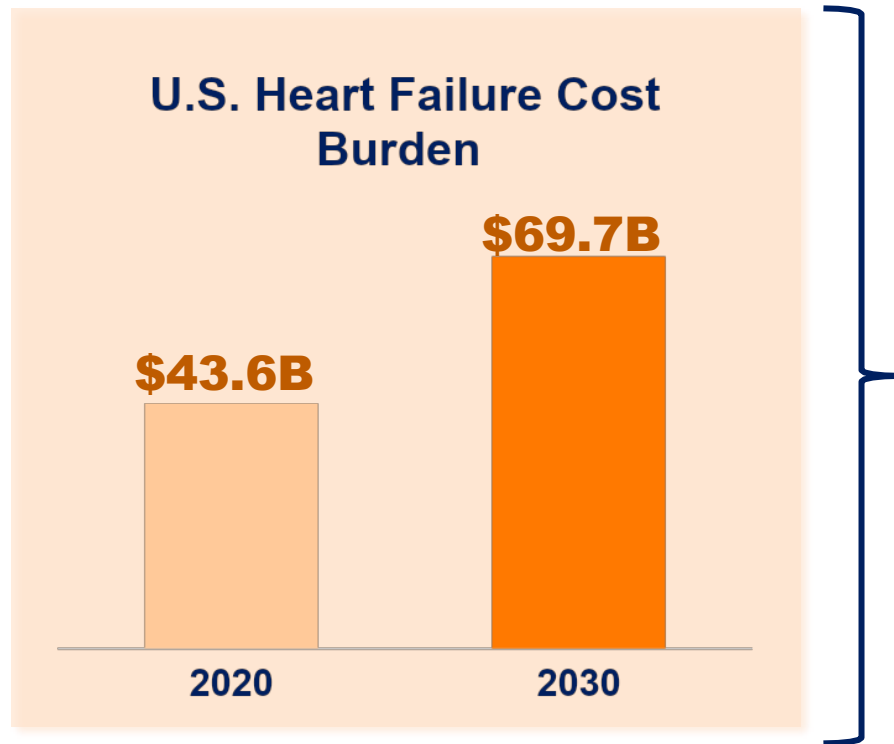
of patients die within 1 year



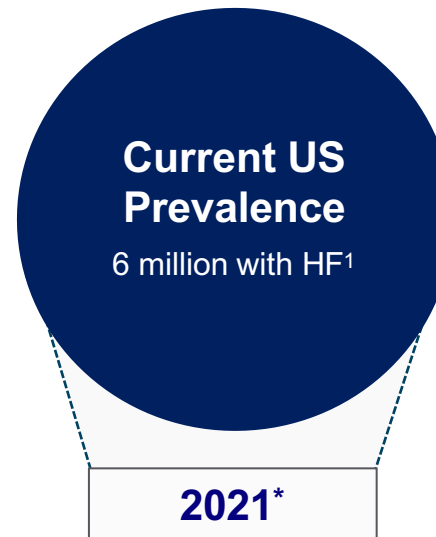
50%

of patients die within 5 years

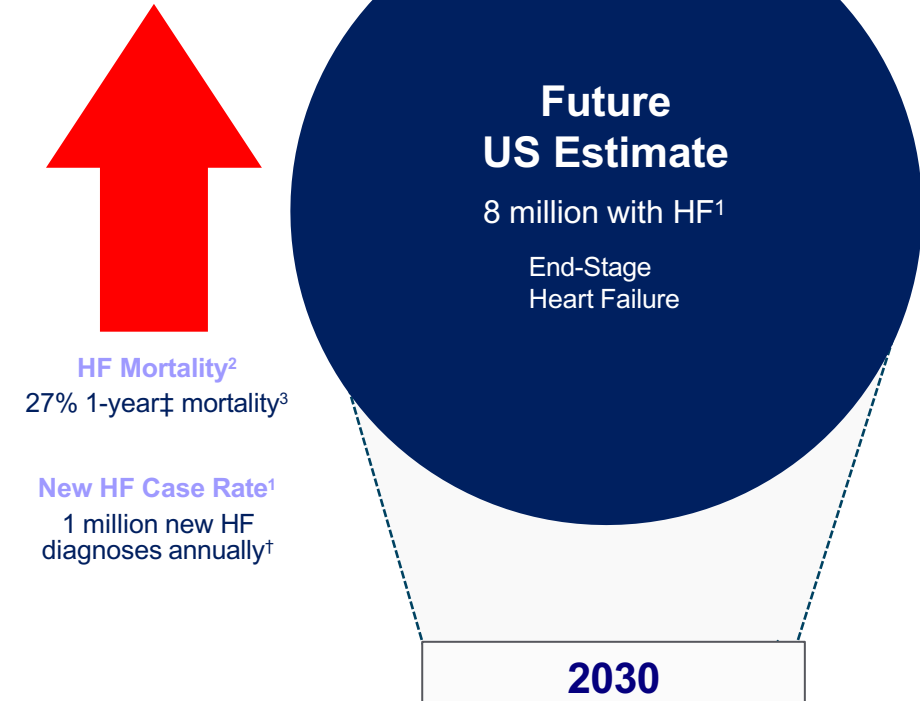
HF Burden in 2030: 33% more Patients, \$70B Cost



1. Virani SS et al. *Circulation* 2021;143(8): e254-e743.
2. CDC WONDER Online Database, released in 2021. <http://wonder.cdc.gov/icd-10.html>. Accessed February 1, 2022.
3. Lin AH et al. *Mil Med* 2017;182(9):e1932-e1937.

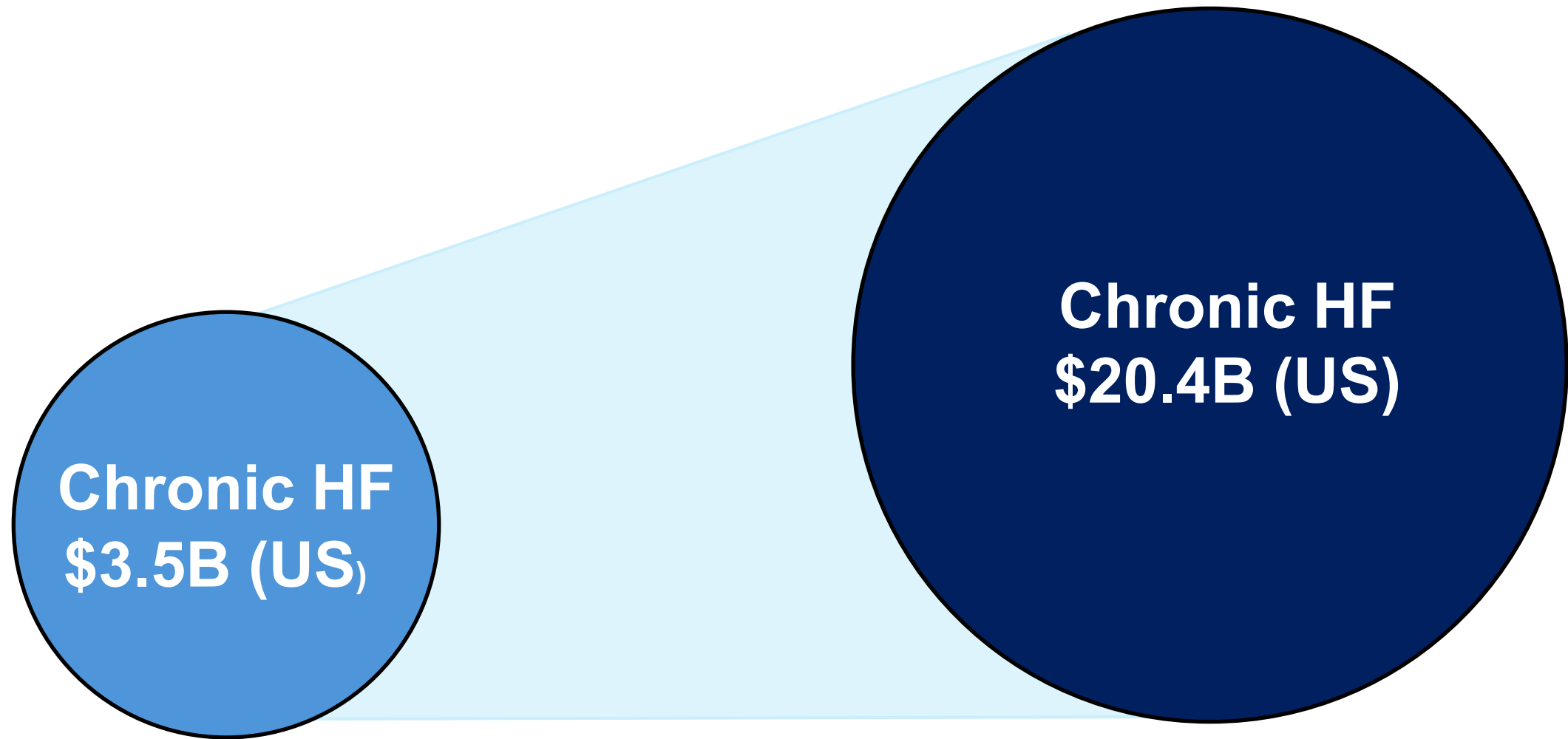


- *Based on NHANES 2015-2018 data.
†Based on ARIC Surveillance 2014 data for adults ≥55 years of age.
‡Based on US Department of Defense MHS MDR data 2007-2011.



ARIC=Atherosclerosis Risk in Communities; CDC=Centers for Disease Control and Prevention; HF=heart failure; MDR=Military Data Repository; MHS=Military Health System; NHANES=National Health and Nutrition Examination Survey.

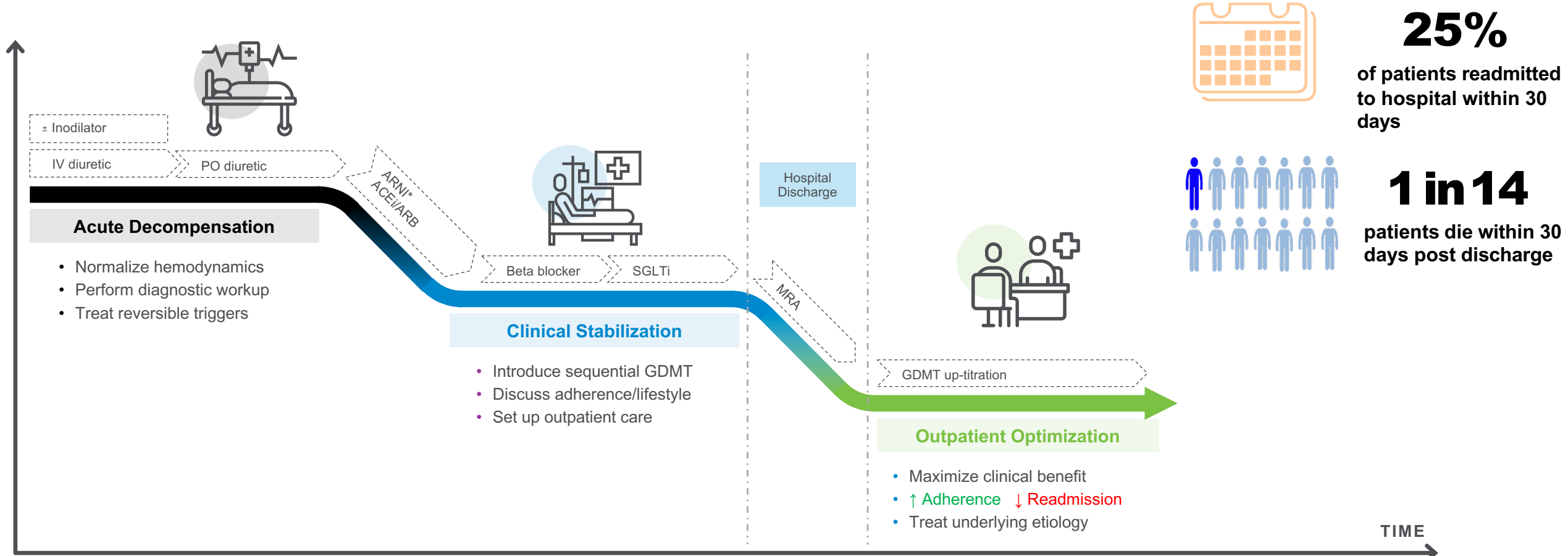
Heart Failure (HF) Market Opportunity



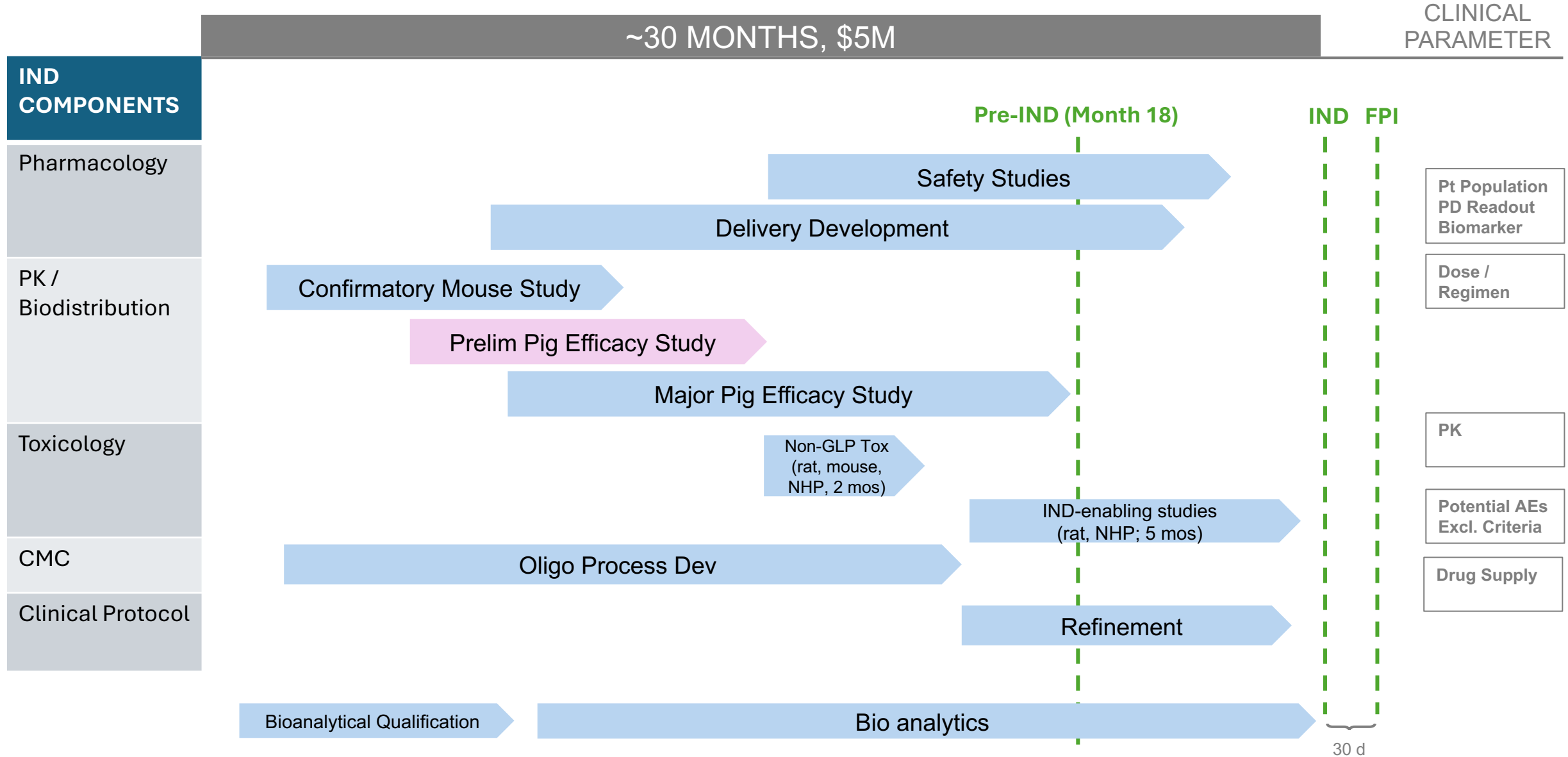
**2018
Gross Sales**

**2035 Forecasted
Gross Sales**

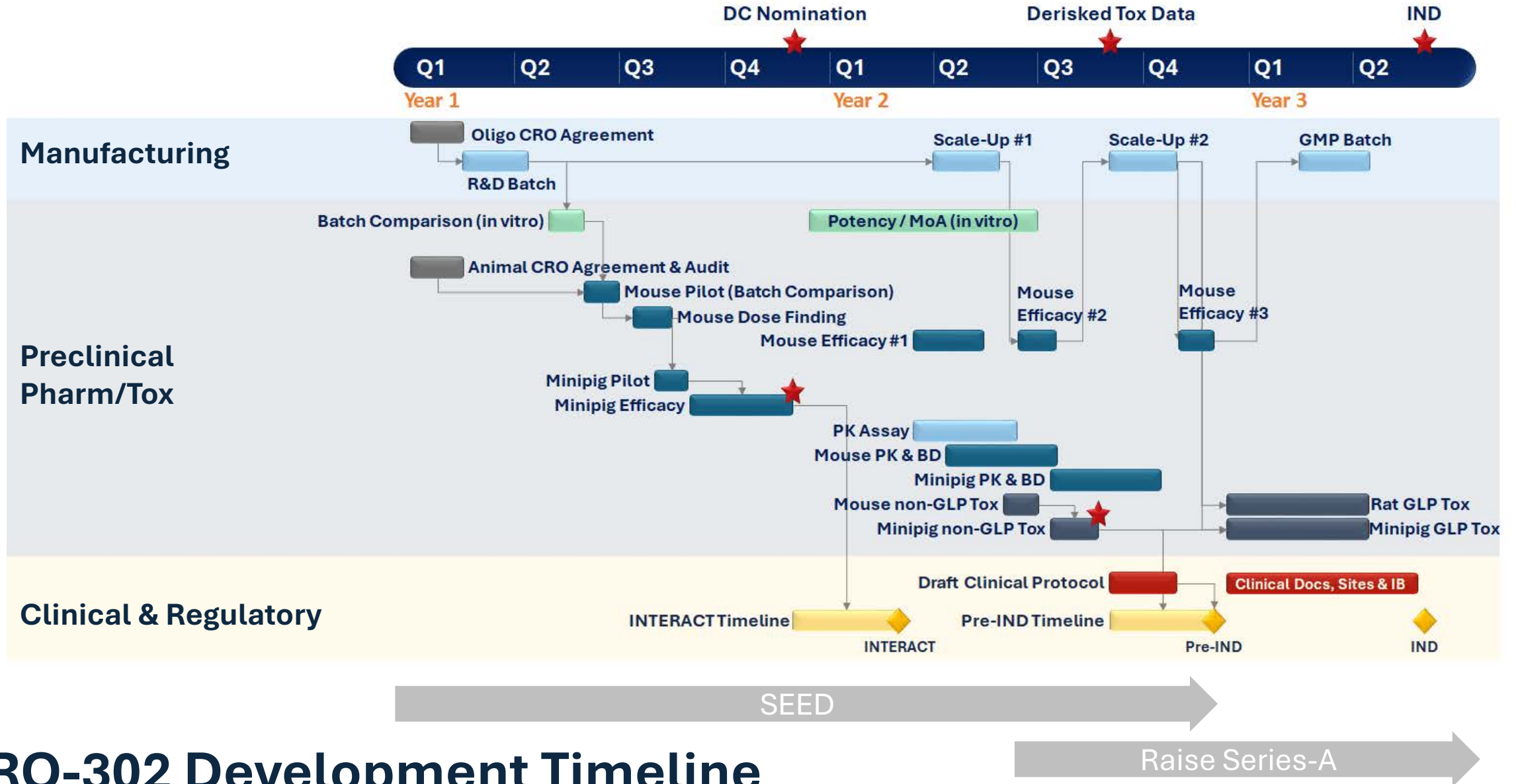
Patient Journey: Hospitalization to Discharge



Regulatory/Development Plan



PRO-302 Development Timeline



Pre-Clinical Funding & Use of Funds

\$5,000,000 Raise

- \$5,000,000 Total Raise
- Traditional Convertible Note
- Conversion to Series A terms

Use of Funds

- Expanded Pig Study
- Pharmacology & Toxicology Models
- PK / PD Analysis
- Chemical Manufacturing Controls (CMC)
- Delivery Mechanism of PRO302
- Regulatory Analysis
- Expansion of Prolifagen IP Portfolio

Next Steps

Business Development

- Continue De-Risking Pathway
- Execute Development Strategy
- Safety & Efficacy in Large Animal Study
- Manufacturing Pathway
- Next Generation Oligo Discovery
- Expansion of IP Portfolio
- Delivery Mechanism for PRO-302

Strategic Partnership

- Market Leader
- Complimentary Market
- Equity Investment
- Milestone-Based Funding
- Access to Prolifagen Platform

Why Invest in Prolifagen?

- Experienced Team with a Proven Record of Success
- Solution for a Significant Unmet Need
- Ahead of the Curve with miRNA Technology
- Cardiology Existing Market and miRNA Emerging Market
- Exit Potential





PROLIFERATE. REGENERATE. RESTORE.

A Pennsylvania Biotechnology Center Company

THANK YOU

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PROLIFERATE. REGENERATE. RESTORE.