VentriGel Case Study: A myocardial ECM hydrogel for treating ischemic cardiomyopathy

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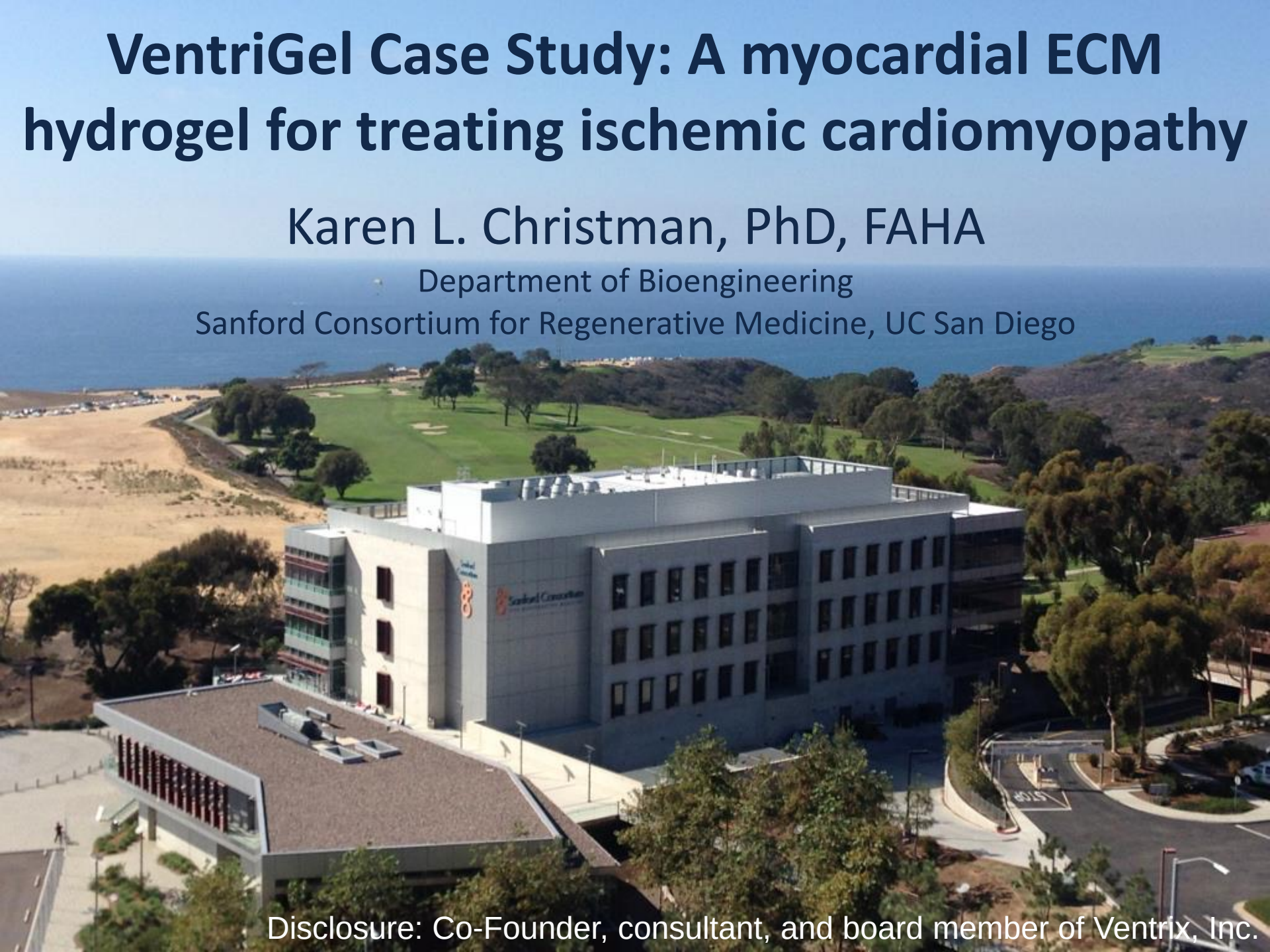
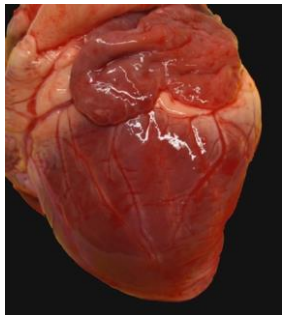
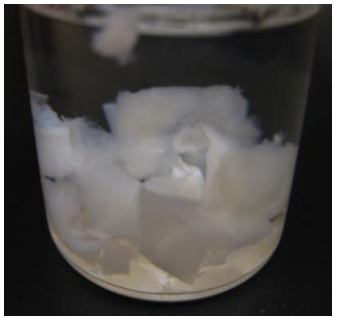


Disclosure: Co-Founder, consultant, and board member of Ventrix, Inc.

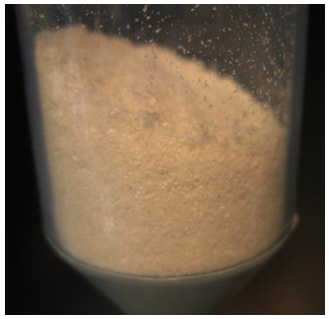
VentriGel



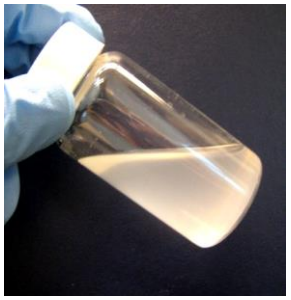
Porcine Heart



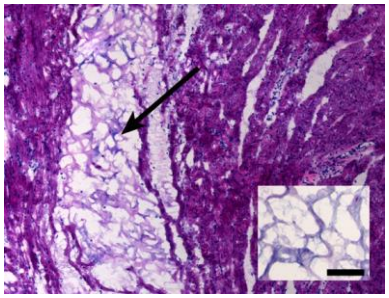
Decellularized cardiac ECM

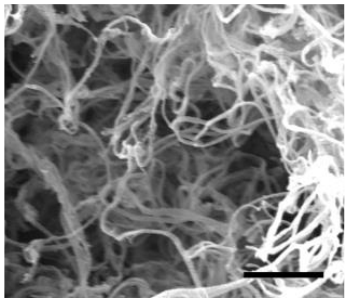


Lyophilized, milled ECM



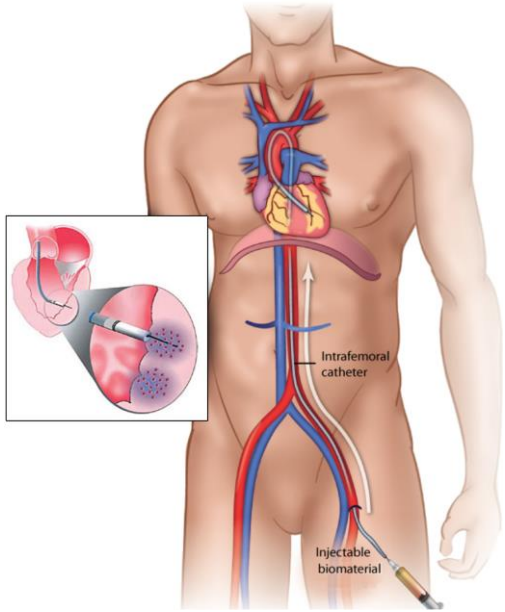
Liquid matrix





In vivo self-assembly

1 µm



Singelyn, DeQuach et al, *Biomaterials* 2009

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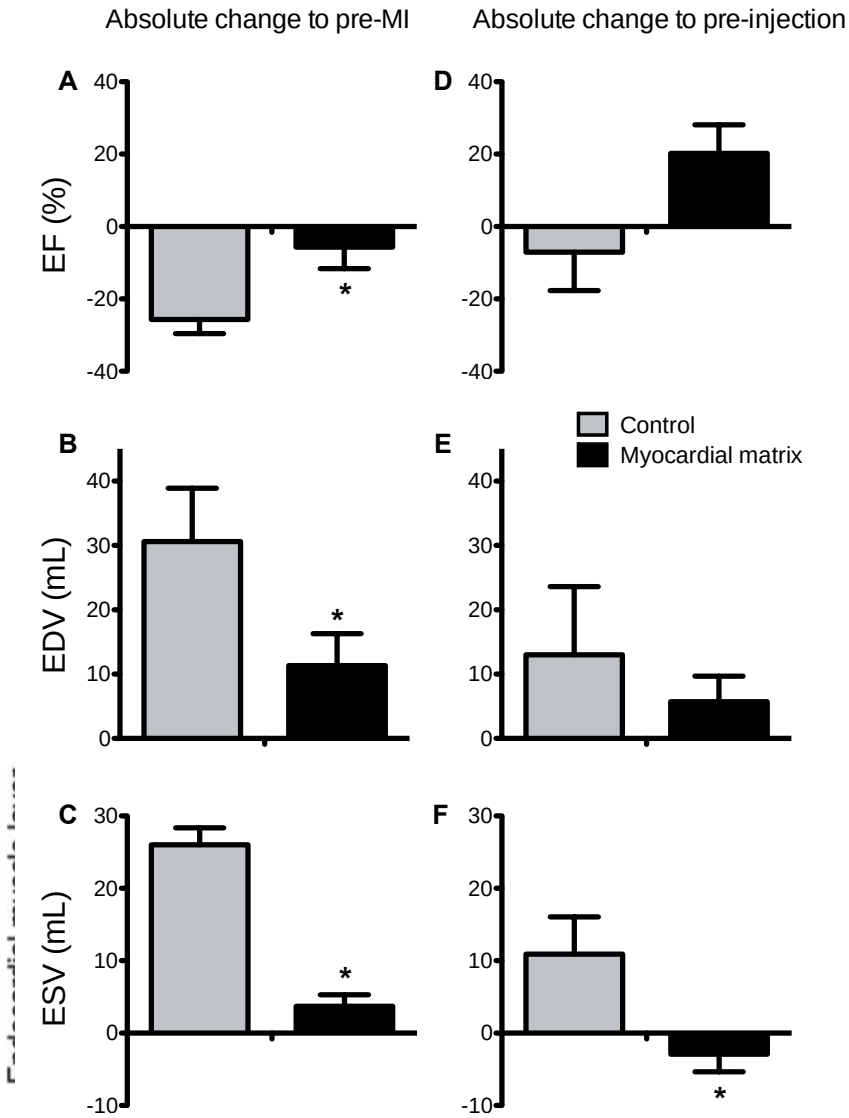
VentriGel Improves Cardiac Function Post-MI

- Improved global and regional cardiac function in porcine MI model
- Decreased left ventricular end-systolic and end-diastolic volumes
- Complex mechanism of action
- Increased cardiac muscle and reduce fibrosis



Seif-Naraghi et al, *Science Translational Medicine,* 2013; Singelyn et al, *JACC 2012;* Wassenaar et al, *JACC*, 2016

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Phase 1: Study Design

Title: CV-201 - A Study of VentriGel in Early and Late Post-myocardial Infarction Patients

Subjects: 15 subjects (all treated)

Patients: Index MI 60 days to 3 years prior and treated with PCI

25%<EF<45% (by echo and cMR)

Delivery: Catheter, transendocardial delivery via NOGA/Myostar catheter

Assessments: At baseline, 3 and 6 months

Cardiac MR, 6MWT, NYHA Functional classification, MLWHFQ, BNP

Duration: 12 months with visits at baseline, 1, 2, 4, 12 and 24 weeks
Phone call at 12 months

Safety: Adverse events, SAEs, clinical chemistries, vital signs
TTEM, Holter monitoring, 12-lead ECG

Efficacy: Change from baseline: EF, ESV, EDV, infarct size, viable tissue, perfusion, BNP, 6MWT, MLWHFQ

ClinicalTrials.gov Identifier: NCT02305602

Phase 1 Results

15 patients treated with VentriGel

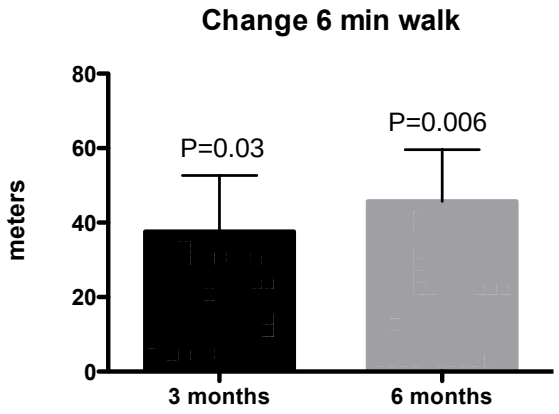
Primary Endpoint: Safety:

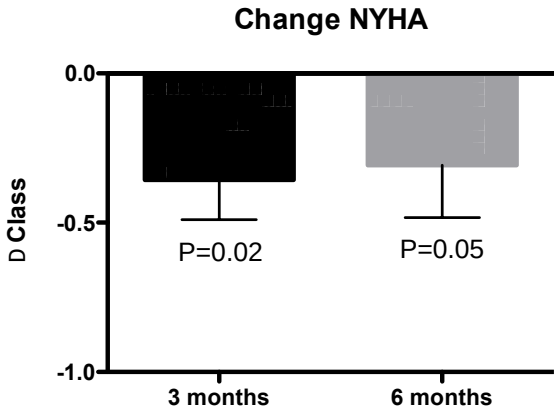
VentriGel has been well-tolerated

Secondary Endpoints:

Encouraging efficacy signals

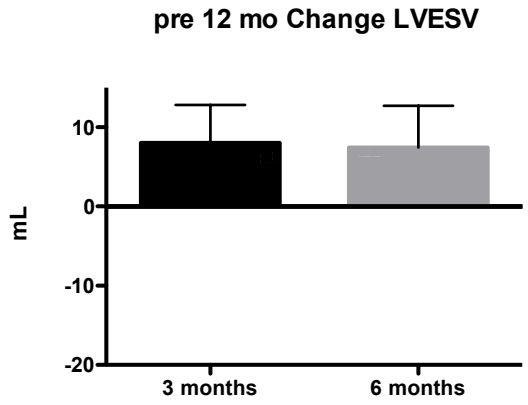
- Statistically significant improvements in 6 min walk test
- Symptoms score trending toward improvement
- 10 out of 14 improved in ESV or EDV on cMR

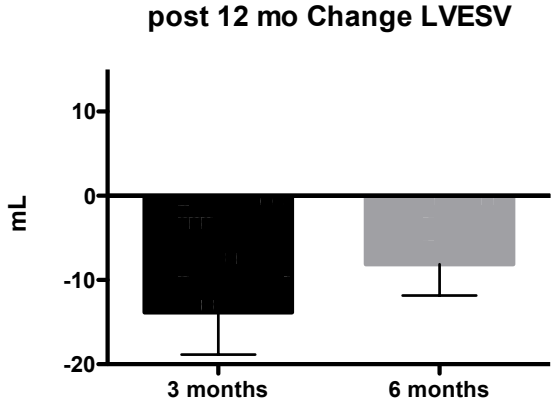


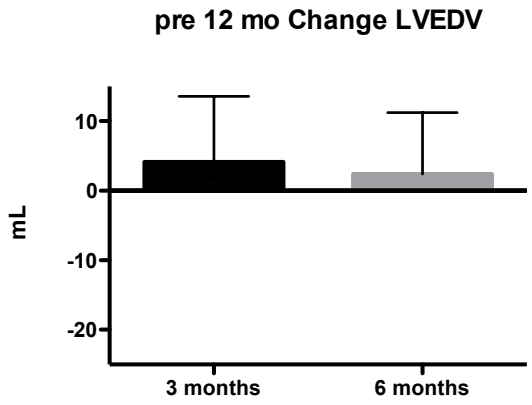


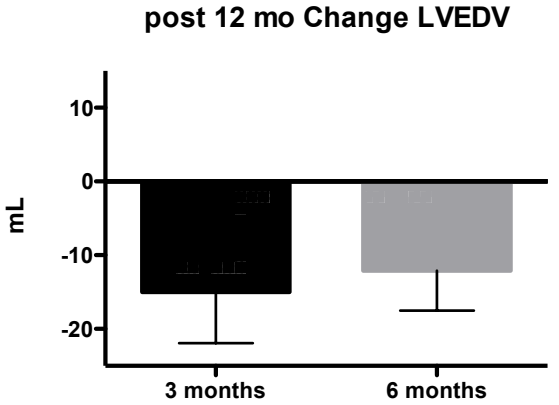
Early vs. Late MI Patients

Ventrix CV-201				
Row	Identifier	Age/ Gender	Months post-MI	NYHA Base
1	02/206	65/M	35.5	1
2	02/203	67/M	35	2
3	02/201	59/M	23	1
4	02/205	59/M	22	3
5	04/403	46/M	20	1
6	07/702	56/M	18	2
7	03/301	69/M	14	2
8	01/104	67/F	11	2
9	06/601	46/F	11	2
10	04/404	62/M	8.5	3
11	02/207	62/M	7	1
12	03/304	45/M	6	2
13	01/103	69/F	4	2
14	04/401	51/F	4	2
15	04/402	63/M	3	2









Disease Severity

Overall improvements at 6 months evident for the whole population

Particularly strong in the 180-300 mL range of LVEDV at Baseline

Population	EDV	ESV	6MWT	NYHA	MLWHFQ	BNP	Scar	Viable	Scar%
All	+	0	+	+	+	-	-	+	-
LVEDV<180	0	-	+	+	-	-	+	+	+
LVEDV 180-300	+	+	+	+	+	+	0	+	+
LVEDV>300	-	-	+	+	+	-	-	-	-

Legend

+	improved (i.e. decreased in: EDV, ESV, NYHA, MLWHFQ, BNP; increased: 6MWT)
0	no change
-	worsened (i.e. Increased in: EDV, ESV, NYHA, MLWHFQ, BNP; decreased: 6MWT)

Challenges on Regulatory Approval Pathway

- Complex Mechanism of Action

↓ cell death

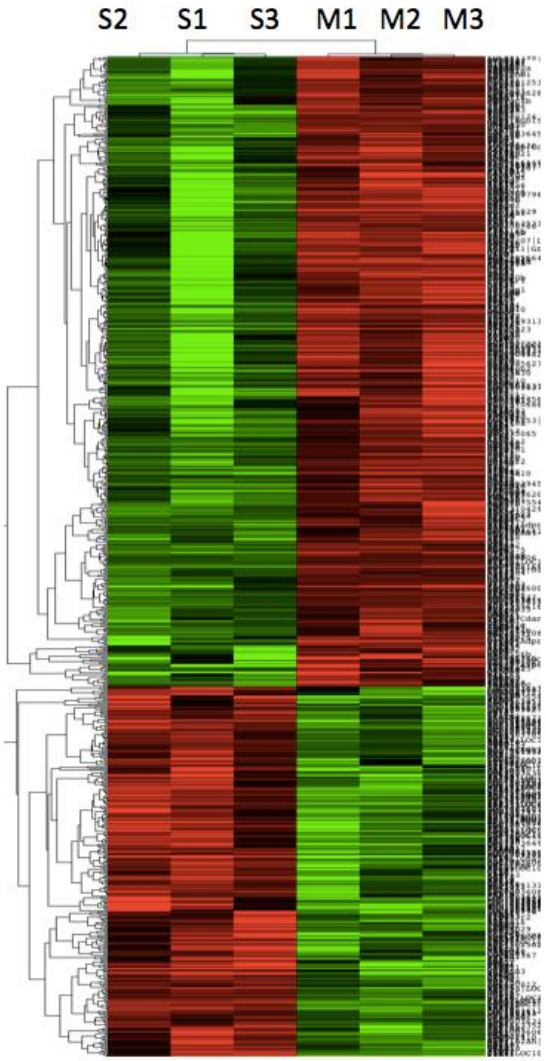
↓ hypertrophy

↑ immunomodulatory response

↑ metabolic processes

↑ blood vessel development

↑ heart development



Wassenaar et al, *JACC*, 2016

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Challenges on Regulatory Approval Pathway

- Need activity assay for Phase III and approval
  - How does one adequately show bioactivity with a simple in vitro assay when there is a complex mechanism of action?
    - Variability with regenerative medicine products
    - Variability with cells in culture
    - No direct link to activity *in vivo*
- Difficult to develop antibody assays for complex products
- Given good safety profiles, more leeway is needed on approvable endpoints
  - Post-market monitoring to better understand efficacy with a large more variable population

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