RENOVACOR

Transformative Therapies for BAG3-Associated Diseases

August 2021

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Forward Looking Statements

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Industry and Market Data

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RENOVACOR

About the Transaction

Transaction Overview: Proposed Merger of Renovacor and CHAQ[1]

Renovacor, Inc. ("Renovacor") is expected to combine with Chardan Healthcare Acquisition 2 Corp. ("CHAQ") to create a publicly-listed, innovative gene therapy company

- Renovacor is a novel AAV-based gene therapy platform targeting diseases resulting from *BAG3* gene dysfunction with primary focus on rare cardiovascular disease

Key Transaction Terms

- **CHAQ to issue 6.5 million common shares[2] to Renovacor equityholders**, with pre-money valuation of $65 million[2] and post transaction equity value of approximately $198 million[3]
- **Strong incentive structure facilitated by earn-out provisions,** providing Renovacor equityholders and Chardan with additional upside upon realizing share price based milestones
  - 2.0 million earn-out shares for Renovacor existing equityholders, to be delivered in 3 installments if the share price exceeds $17.50, $25.00 and $35.00 per share by CYE-2023, CYE-2025 and CYE-2027, respectively[4]
  - 0.5 million earn-out shares (with identical terms) for Chardan, which agreed to shift an equivalent number of Founder Shares to earn-out shares, in order to further align sponsor interests
- Approximately **$116 million of gross proceeds is expected to be raised, funded by $30M PIPE investment and $86M in CHAQ Trust (assuming no redemptions are effected)**
  - $30M from PIPE investment subscribed by Chardan, RTW Investments, Surveyor Capital (an affiliate of Citadel), Acorn Bioventures, Longview Ventures (an affiliate of Broadview Ventures) and Innogest Capital
  - Approximately $50M additional capital can be raised upon the exercise of CHAQ public warrants upon realizing requisite share price[5]
- **Pro forma cash to provide cash runway into end of 2023**; which can be further extended to 1H-2024 upon exercise of CHAQ public warrants[5]
- **Renovacor existing equityholders to own approximately 42% of the pro forma entity** at transaction close[6], taking into account rollover of a 100% of vested equity and $17.5M of new investment by Renovacor existing equityholders
- **Transaction expected to close by Q3 2021**

Summary Transaction Terms

(US$ and shares in M, except per share amounts)

Pro Forma Valuation At Close	
Share Price	$10.0
Pro Forma Shares Outstanding	19.8
Pro Forma Equity Value [2]	**$197.8**
Less: Pro Forma Net Cash	(113.2)
Pro Forma Transaction Value	**$84.6**

Sources of Funds	
PIPE	$30.0
Cash Held in CHAQ Trust	86.2
Renovacor Shareholder Equity Rollover [1]	65.0
Total	**$181.2**

Uses of Funds	
Equity Issued to Renovacor Shareholders	$65.0
Cash Funding to Renovacor Balance Sheet	113.2
Assumed Transaction Expenses	3.0
Total	**$181.2**

(1) The following description of the proposed merger is only a summary and is qualified in its entirety by reference to the definitive agreement relating to the proposed merger, a copy of which will be filed by CHAQ with the SEC as an exhibit to a Current Report on Form 8-K, which can be accessed through the SEC's website at www.sec.gov.
(2) Shares issued as of transaction close, excluding potential future effect of 2.0M earn-out shares to be issued to Renovacor insiders
(3) Based on $65.0M pre-money equity value, gross capital raise of $116.2M (between $30M PIPE and $86M of funds in CHAQ Trust, assuming no redemptions are effected) and approximately $17M equity value of sponsor shares
(4) Earnout milestones based on VWAP during any 20 out of a 30-day period
(5) CHAQ public warrants can be forced called upon stock price hitting $16.0/share with cash exercise to yield approximately $49.5M of cash proceeds
(6) Common share ownership at transaction close excluding the potential future effect of 2.5M total earnout shares, 8.50M public warrants and 3.5M private placement warrants

RENOVACOR

Renovacor Overview

Mission Statement

We are developing a pipeline of innovative and proprietary AAV-based gene therapies for BAG3-associated diseases in areas of high unmet medical needs.

Value Proposition Highlights

Developing single dose REN-001 gene therapy candidate for familial DCM and other diseases due to BAG3 mutation

- Potential to address ~70,000 patients (US + EEA) with familial dilated cardiomyopathy (DCM) due to a mutation in the *BAG3* gene ("BAG3 DCM")[1]
- BAG3 DCM represents a high unmet medical need, due to an average age of onset of 38 years and less than 50% survival 5 years after diagnosis[2]
- BAG3 biology enables a diversified pipeline with multiple follow-on opportunities to pursue development in heart failure and central nervous system diseases

Compelling improvements in cardiac function demonstrated in multiple preclinical models

- REN-001 improved cardiac function in haploinsufficiency DCM mouse, with no deleterious effects seen
- REN-001 restored normal EF phenotype in post-MI mice, and demonstrated improved EF function in a pig post-MI model

Led by experienced management and an exceptional class of cardiovascular disease and gene therapy scientific advisors

- Founded by world renowned cardiovascular scientist (Arthur Feldman, MD, PhD) who has published a variety of articles elucidating the role of BAG3 in disease states
- Anchored by experienced leadership team and scientific advisors that include thought leaders and pioneers in the cardiovascular disease and gene therapy fields

Anticipated IND submission and potential phase I/II trial initiation anticipated in mid-2022

- Development plan incorporates potentially lower-risk features (AAV9, ICr delivery)
- We believe BAG3 DCM provides the potential for orphan and other regulatory designations designed to accelerate development

We believe our BAG3 IP position provides important barriers to entry

- Company vision is to become the leading BAG3 biotech company, based on its formidable IP- and expertise-driven barriers to entry
- 5 IP patent families filed to protect science including for any route of delivery of BAG3; for BAG3 variants; and for BAG3 use in multiple diseases (e.g. CV, CNS)

Backed by strong investor syndicate (experienced in CV and GT) that synergizes with CHAQ

- Existing investors have deep domain expertise and successful track record of early investments in cardiovascular-directed therapies and AAV-based gene therapies
- CHAQ draws on the resources of partner, Chardan (annual genetic medicines conference, AAV-based GT coverage, corporate access, AAV GT company formation, etc.)

(1) Source: Ziaeian and Fonarow 2016; Judge et al., 2008; Hershberger et al., 2010; Haas et al., 2015; Knezevic et al., 2015.
(2) Source: Myers, VD., … Feldman, AM., *JACC Basic Transl Sci,* 2018, 3, 122–131; Dominguez, F. *et al., J Am Coll Cardiol,* 2018, 72, 2471-2481; Aung, N. *et al. Circulation*, 2019, 140, 1318-1330.

We Believe Renovacor's REN-001 is Well Positioned for Success

Monogenic diseases are lower risk for AAV GTs

- Targeting disease with known genetic origin
- BAG3 mutations well-documented as driver in DCM
- Goal is to increase BAG3 levels in DCM subjects

Local (intracoronary retrograde) delivery allows lower total dose

- May reduce burden on manufacturing
- May improve COGS and LT profitability
- Reduces potential for various vector toxicities

Utilizes validated AAV9 capsid

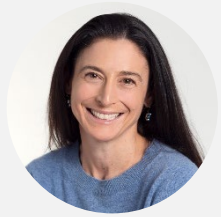
- AAV9 currently used in approved therapies (e.g. Zolgensma)
- AAV9 has demonstrated cardiac tropism
- Has high transduction efficiency
- Non-integrative vector

Non-immunogenic one-time human BAG3 payload

- Therapeutic payload is human *BAG3* gene
- DCM patients are haploinsufficient and produce low levels of native BAG3; therefore, the protein is not foreign and should not elicit an immune response

We believe we have a path to clinic for our lead indication:
The focus on a devastating disease (BAG3 DCM) provides the potential
for orphan and other regulatory designations that could accelerate development

Experienced Leadership Team



Magdalene Cook, MD

President and CEO – Principal, Aisling Capital and Board member of multiple companies

AISLING CAPITAL · COLUMBIA | VAGELOS COLLEGE OF PHYSICIANS AND SURGEONS

Marc Semigran, MD

CMO – 30+ years of experience treating HF and cardiomyopathy; Senior VP of Medical Sciences and CMO at MyoKardia; experience in developing and designing clinical trials for novel therapies for cardiovascular and heart failure/HFpEF

Bristol Myers Squibb · MYOKARDIA · HARVARD MEDICAL SCHOOL · MASSACHUSETTS GENERAL HOSPITAL

Elizabeth White, PhD

CBO and Senior VP, Operations – >30+ years of biotech/pharma experience including in strategy, business development, new product planning, portfolio prioritization in start-ups & large companies

NeuExcell THERAPEUTICS · Pfizer · Wyeth

Jiwen Zhang, PhD

Senior VP, Regulatory Affairs and Quality Assurance – 20+ years of regulatory affairs and quality assurance experience, with >10 years specifically in cell and gene therapy

PassageBio · TMUNITY · Wyeth · SANOFI · GE Healthcare

Wendy DiCicco

Interim CFO – 15+ years expertise in finance, strategy, M&A as well as executive roles in public and private companies

Carmell THERAPEUTICS · EYEPOINT PHARMACEUTICALS · FerGene · CannaPharmaRx Endocannabinoid Science · ExpressCells · Imvax

Marcia Bologna

R&D, Program Lead – 35 years of biotech/pharma experience at Genetics Institute, Wyeth, and Pfizer

Pfizer · GENETICS INSTITUTE · Wyeth

Valerie Myers, PhD

Director, Preclinical Development – 10+ years research in HF signal transduction, with focus on *BAG3*

TEMPLE UNIVERSITY · Jefferson · PennState

Exceptional Scientific Advisors and Board of Directors

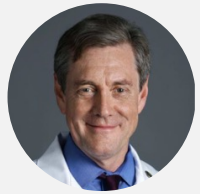
Thought Leaders in Cardiovascular Disease

Arthur Feldman, MD, PhD

- Renovacor, Founder and Chair of SAB
- Laura H. Carnell Prof. of Medicine, Temple
- Former Chief of Cardiology UPMC
- Past President HFSA, Assoc. of Professors of Cardiology
- Lifetime Achievement Award, HFSA; Distinguished Scientist Award ACC, 2019

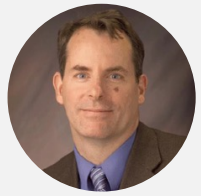
Michael Bristow, MD, PhD

- Prof. of Medicine and former Head of Cardiology, Univ. of Colorado Health Sciences
- Co-founder, President and CEO, ARCA Biopharma
- Founder, Myogen
- Lifetime Achievement Award, HFSA
- Credited with development of science and clinical utility of β-blockers for HF



Douglas Mann, MD

- Lewin Prof. of Medicine, former Director of Cardiovascular Div., Washington University School of Medicine
- Past President, HFSA
- Lifetime Achievement Award, HFSA
- Editor-in-Chief, JACC Basic Translational Science



Dennis McNamara, MD

- Prof. of Medicine and Dir. of the Heart Failure Research Center, UPMC
- Leading expert in the genetics of dilated and hypertrophic cardiomyopathy
- National Principal Investigator – IMAC I, II & III; GRAFH I & II

Experts in Gene Therapy R&D

Joseph Glorioso III, PhD

- Prof. in the Dept. of Microbiology and Molecular Genetics, UPMC
- Founding member and past president of the American Society of Gene Therapy
- Co-founder and Chair of Scientific Advisory Board at Oncorus, Inc. and Coda Biotherapeutics

Philip Johnson, MD

- CEO, Iterius Biotherapeutics
- >30 various roles in academia, biotechnology sector and venture capital
- Considered an international leader in viral vector technology; invented methods for producing and manufacturing viral vectors and novel capsids
- Past President & CSO at Limelight Bio
- Past Professor and Executive VP & CSO, The Children's Hospital of Philadelphia; past President, Children's Research Institute at Nationwide Children's Hospital

Board of Directors

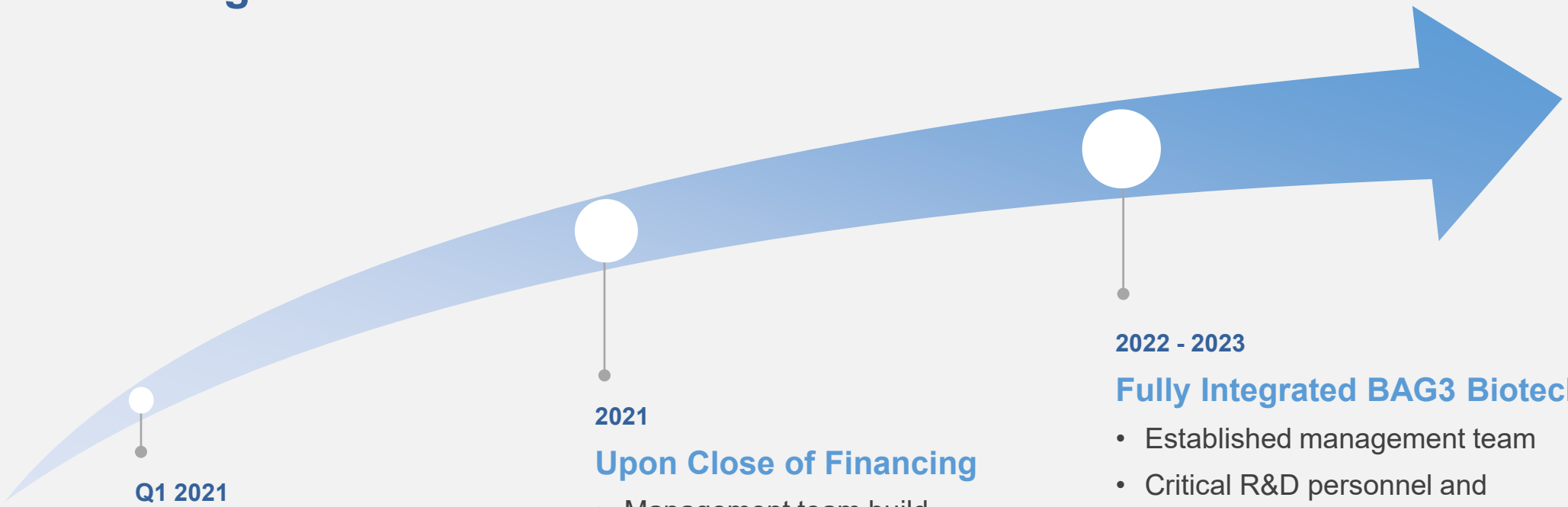
Edward Benz, Jr., MD – President & CEO Emeritus, the Dana-Farber Cancer Institute

Magdalene Cook, MD – Renovacor CEO

Arthur Feldman, MD, PhD – Renovacor Founder; Professor Temple University

Thomas Needham, MBA – Broadview Ventures

Vision: To Develop AAV-based Therapies for *BAG3*-Associated Diseases in Areas of High Unmet Medical Need



Q1 2021

Today

- Lead rare disease program has path to IND
- Genetic model replicates human *BAG3*-associated DCM
- Early R&D for expanded BAG3 pipeline

2021

Upon Close of Financing

- Management team build
- R&D and manufacturing team build
- REN-001 phase I/II preparation
- REN-001 clinical and commercial manufacturing
- BAG3 pipeline expansion work

2022 - 2023

Fully Integrated BAG3 Biotech

- Established management team
- Critical R&D personnel and capabilities established
- Anticipated submission of IND for REN-001
- Anticipated start of REN-001 clinical study
- We expect to expand our BAG3 pipeline asset by progressing to second IND filing

We Expect 1st IND Submission and Phase I/II Initiation in Mid-2022

	Program	Potential Indication	Research / Discovery	Preclinical	IND Submission (Anticipated)	Phase I	Phase II	Phase III	Global Commercial Rights
Heart Failure (DCM)	REN-001 (AAV9-*BAG3*) [ICr]	*BAG3*-associated dilated cardiomyopathy (DCM)			Mid-2022				RENOVACOR Transformative Therapies for BAG3-Associated Diseases
Heart Failure (DCM)	AAV-*BAG3* [IV]	*BAG3*-associated dilated cardiomyopathy (DCM)							RENOVACOR Transformative Therapies for BAG3-Associated Diseases
Other Indications	AAV-*BAG3*	Undisclosed CV indication							RENOVACOR Transformative Therapies for BAG3-Associated Diseases
Other Indications	AAV-*BAG3*	Undisclosed CNS indication							RENOVACOR Transformative Therapies for BAG3-Associated Diseases

Completed

Definitions: **ICr** = intracoronary retrograde infusion; **IV** = intravenous

We Believe Broad BAG3 IP Filed to Provide Renovacor High Barriers to Entry

Patent Family	Countries	Status
BAG3 AS A TARGET FOR THERAPY OF HEART FAILURE	US, EU, CA, JP	Pending
BAG3 COMPOSITIONS AND METHODS	US, EU, HK	Pending
ISCHEMIA/ RE-PERFUSION INJURY	US, EU, AU, CA, CN, IN, IL, JP, MX, KR, HK	Pending
OPTIMIZING BAG3 GENE THERAPY	PCT	Published
BAG3 AND PROTEIN QUALITY CONTROL IN THE BRAIN	US (provisional)	Pending

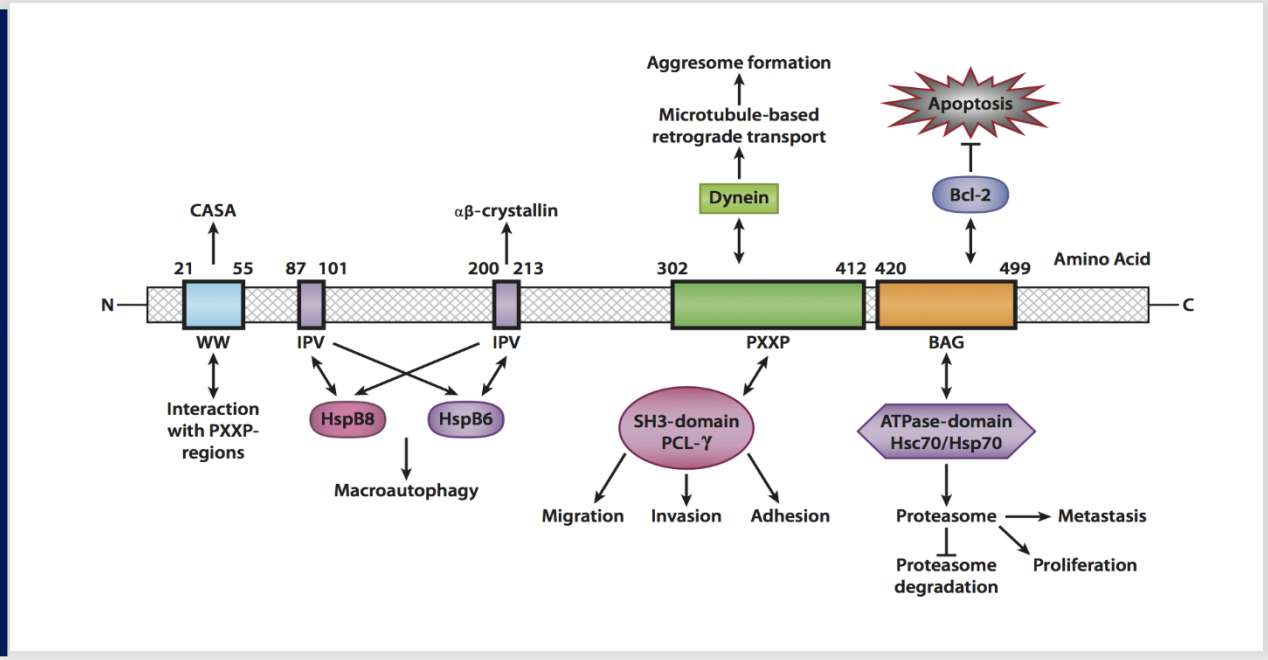
RENOVACOR

Preclinical Studies: Renovacor's REN-001 for Dilated Cardiomyopathy (DCM)

BAG3 Regulates Major Cell Pathways in the Heart

Normal cardiovascular function is dependent on levels of BAG3 protein

BAG3 structure showing its protein binding domains

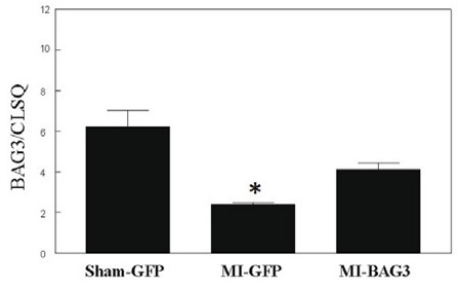


Anti-apoptosis	Protein quality control	Structural support	Cardiac contractility
Inhibits apoptosis (programmed cell death) through binding of Bcl2	Facilitates autophagy as a co-chaperone with heat shock proteins	Provides support for sarcomere through linking actin myofibrils with Z-disc	Enhances contractility by linking β-adrenergic receptor and L-type Ca^{2+} channel

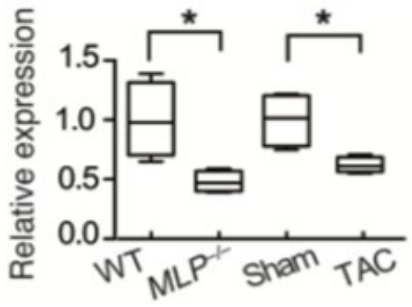
Source: Myers VD., … Feldman AM., *J Am Coll Cardiol Basic Trans Science* 2018, 3, 122–31

BAG3 Protein is Decreased in Mammalian Heart Failure

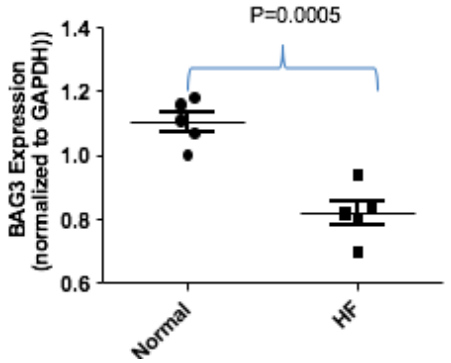
Post-MI mouse



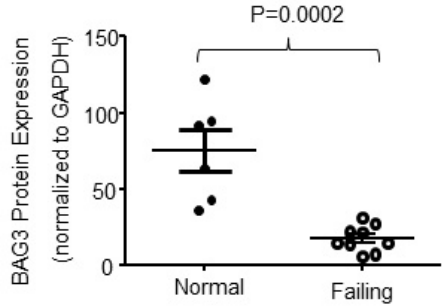
MLP$^{-/-}$ and TAC mice



Post-MI pig



HF humans



Renovacor's goal is to increase BAG3 levels in the heart, thus modifying the disease

Notes: * p<0.05 between MI-GFP and Sham-GFP, and between wild-type / sham and MLP$^{-/-}$ / TAC mice; REN-001 (AAV9-BAG3) dose = 4×10^{12} genome copies (gc)
Source: Feldman *et al.,* 2016; Knezevic, T., … Feldman, AM., *Heart Fail Rev.* 2015, 20, 423–434; Fang, X., *et al., J Clin Invest.,* 2017,-127, 3189-3200; Knezevic, T., … Feldman, AM., *JACC Basic Transl Sci.* 2016, 1, 647–656.

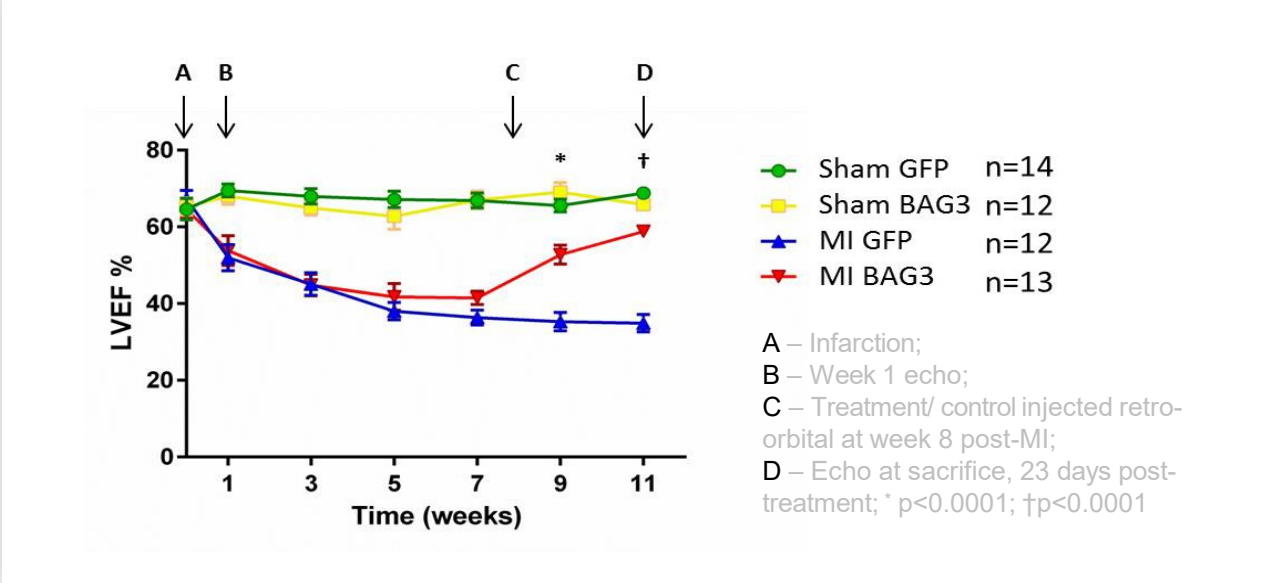
REN-001 Restored Healthy Phenotype in Post-MI Mouse Model

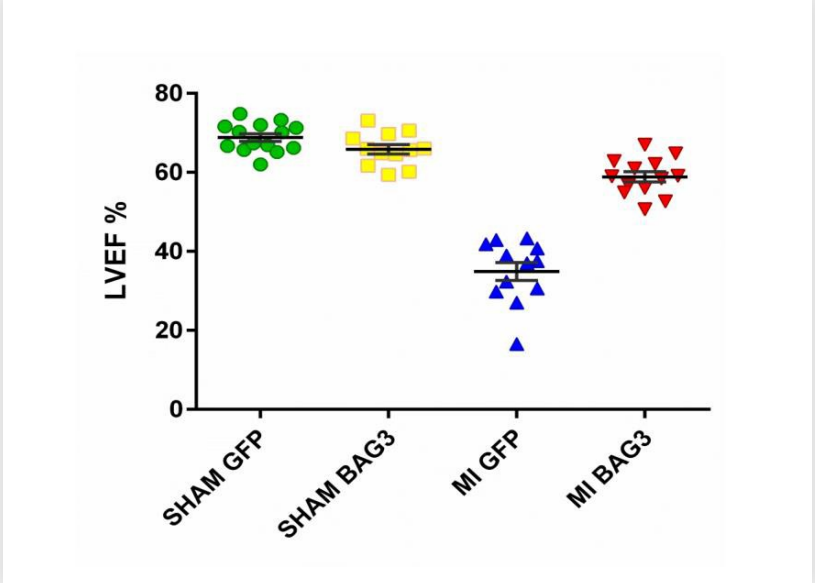
Aim

To asses whether the administration of REN-001 improves left ventricular (LV) function in mouse model of DCM

Methods

- 8-week old male c57BL/6 mice randomized to myocardial infarction (MI) induction via left coronary artery ligation or sham procedure
- Mice in each group then randomized to received either gene therapy with *BAG3* or *GFP* [dose = 4×10^{12} genome copies (gc)]



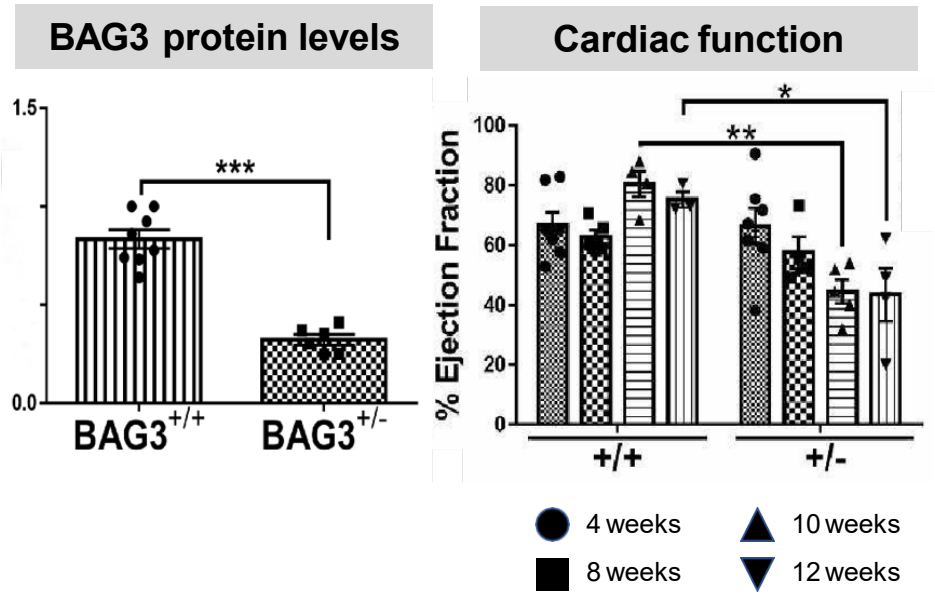


[1](1) Mice developed a DCM phenotype; (2) REN-001 restored normal ejection fraction in post-MI mice; and (3) BAG3 overexpression exhibited no safety concerns due to autoregulation[2]

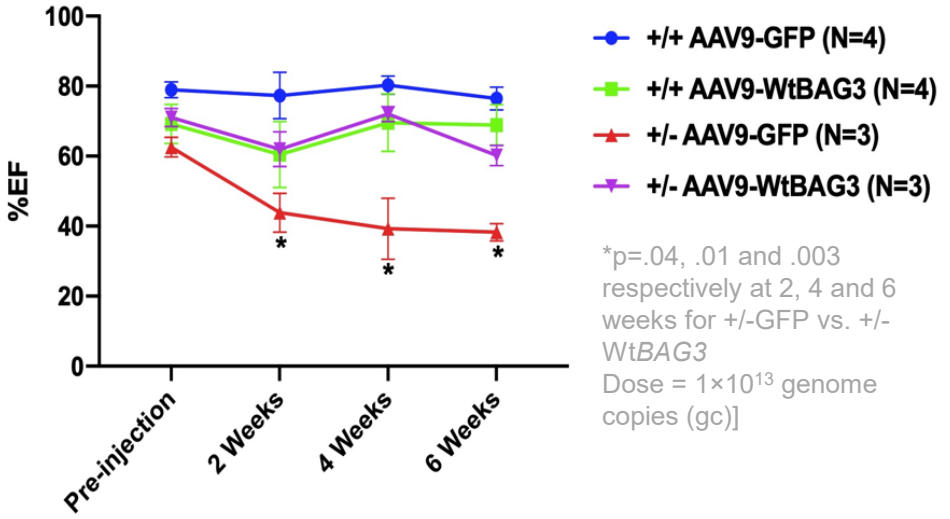
Source: [1]Knezevic T.,… Feldman, A.M., *J Am Coll Cardiol Basic Trans Science*. 2016, 1, 647–56; [2]Gentilella, A. & Khalili, K., *J Cell Biochem. 2009,* 108, 1117–1124.

REN-001 Showed Durable Rescue in DCM Haploinsufficiency Model

BAG3$^{+/-}$ mouse model demonstrated BAG3 haploinsufficiency and DCM phenotype



Administration of REN-001 rescued dilated cardiomyopathy (DCM) phenotype



*p=.04, .01 and .003 respectively at 2, 4 and 6 weeks for +/-GFP vs. +/-Wt*BAG3*
Dose = 1×10^{13} genome copies (gc)]

Administration of REN-001 in a BAG3 DCM haploinsufficiency mouse model rescued DCM phenotype

Sources: Haploinsufficiency data published in Myers VD., … Feldman AM., *J Cell Physiol.* 2018; 233: 6319– 6326. *REN-001 administration adapted from data published in* Myers VD., … Feldman AM., *JAMA Cardiol.* 2018; 3(10):929-938 and unpublished data from the Feldman lab.

We Believe the Role of BAG3 Extends Beyond Dilated Cardiomyopathy

BAG3 is implicated in many diseases including heart failure, cardiac amyloidosis and CNS disorders

The Feldman group continues to be at the forefront of elucidating the biology and mechanism of BAG3

Feldman group

JCI insight

Bcl-2–associated athanogene 3 protects the heart from ischemia/reperfusion injury

Feifei Su, … , Joseph Y. Cheung, Arthur M. Feldman

Feldman *et al.*

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BAG3 regulates contractility and Ca^{2+} homeostasis in adult mouse ventricular myocytes

Arthur M. Feldman [b,c], Jennifer Gordon [d], JuFang Wang [a], Jianliang Song [a], Xue-Qian Zhang [a], Valerie D. Myers [c], Douglas G. Tilley [a], Erhe Gao [a], Nicholas E. Hoffman [a], Dhanendra Tomar [a], Muniswamy Madesh [a], Joseph Rabinowitz [a], Walter J. Koch [a], Feifei Su [c,e], Kamel Khalili [d], Joseph Y. Cheung [a,b,*]

Feldman group

BAG3: a new player in the heart failure paradigm

Tijana Knezevic, Valerie D. Myers, Jennifer Gordon, Douglas G. Tilley, Thomas E. Sharp III, JuFang Wang, Kamel Khalili, Joseph Y. Cheung & Arthur M. Feldman

Heart Failure Reviews **20**, 423–434(2015) | Cite this article

Annals of NEUROLOGY — An Official Journal of the American Neurological Association and the Child Neurology Society

Original Article

Mutation in *BAG3* causes severe dominant childhood muscular dystrophy†

Duygu Selcen MD, Francesco Muntoni MD, Barbara K. Burton MD, Elena Pegoraro MD, Caroline Sewry PhD, Anna V. Bite BA, Andrew G. Engel MD

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BAG3 plays a central role in proteostasis in the heart

Wataru Mizushima and Junichi Sadoshima

Cell Tissue Res (2017) 368:249–258

DOI 10.1007/s00441-017-2570-7

REGULAR ARTICLE

BAG3 is involved in neuronal differentiation and migration

Antonietta Santoro [1] · Vanessa Nicolin [2] · Fulvio Florenzano [3] · Alessandra Rosati [1] · Mario Capunzo [1] · Stefania L. Nori [1]

BAG3 facilitates the clearance of endogenous tau in primary neurons

Zhinian Lei [1], Corey Brizzee, Gail V.W. Johnson

Article | Open Access | Published: 17 December 2018

Myopathy associated BAG3 mutations lead to protein aggregation by stalling Hsp70 networks

Melanie Meister-Broekema, Rebecca Freilich, Chandhuru Jagadeesan, Jennifer N. Rauch, Rocio Bengoechea, William W. Motley, E. F. Elsiena Kuiper, Melania Minoia, Gabriel V. Furtado, Maria A. W. H. van Waarde, Shawn J. Bird, Adriana Rebelo, Stephan Zuchner, Peter Pytel, Steven S. Scherer, Federica F. Morelli, Serena Carra, Conrad C. Weihl, Steven Bergink, Jason E. Gestwicki & Harm H. Kampinga

Nature Communications **9**, Article number: 5342 (2018) | Cite this article

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Background: *BAG3*-associated Dilated Cardiomyopathy (DCM)

BAG3-Associated DCM: The Biology is Well Understood

Mutations in BAG3 lead to DCM; the phenotype in animal models rescued by REN-001

- ***BAG3* gene** is highly conserved and encodes for a multifunctional protein due to multiple domains
- **BAG3** is highly expressed in the heart and muscle
- Mutations in ***BAG3*** lead to familial DCM due to a decrease in BAG3 protein in the heart
- **BAG3** insufficiency in animal models leads to ventricular dysfunction
- ***BAG3*** knockdown in genetic animal model (haploinsufficient model) leads to decreased BAG3 levels exhibiting disease phenotype
- Treatment of haploinsufficient model of disease with *BAG3* gene therapy normalizes BAG3 levels and cardiac function
- **REN-001** significantly enhanced left ventricular function and decreased infarct size in mice

Source: Myers, VD., … Feldman, AM., *JACC Basic Transl Sci,* 2018, 3, 122–131; Dominguez, F. *et al., J Am Coll Cardiol,* 2018, 72, 2471-2481; Aung, N. *et al. Circulation*, 2019, 140, 1318-1330.

BAG3-Associated DCM: <5 Year Survival after Disease Onset[1]

DCM resulting from BAG3 deficiency is an area of high unmet medical need

#3
Most common cause of familial DCM

~70,000
Patients in the US + EEA

38 yrs
Average age of onset of disease

80%
Penetrance in patients >40 years

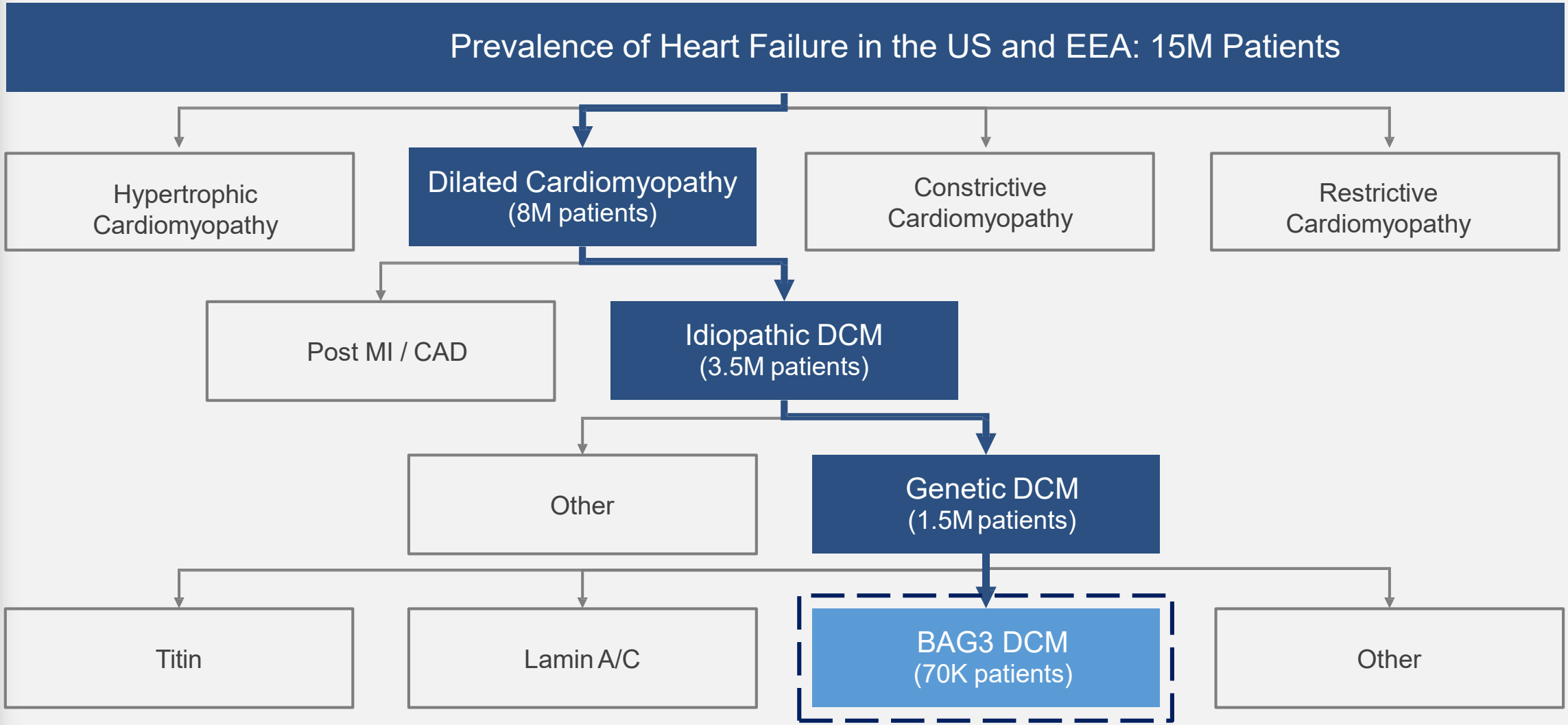
< 50%
Of affected individuals will survive >5 years after disease onset

DCM disease progression is more rapid in patients with *BAG3* mutations versus individuals having ischemic disease

(1) Givertz M & Mann DL. Epidemiology and natural history of recovery of left ventricular function in recent onset dilated cardiomyopathies. Curr. Heart Fail. Reports. 2013, 10: 321-220.

Source: Myers, VD., … Feldman, AM., *JACC Basic Transl Sci,* 2018, 3, 122–131; Dominguez, F. *et al., J Am Coll Cardiol,* 2018, 72, 2471-2481; Aung, N. *et al. Circulation*, 2019, 140, 1318-1330; Knezevic, T., V. D. Myers, J. Gordon, D. G. Tilley, T. E. Sharp, 3rd, J. Wang, K. Khalili, J. Y. Cheung and A. M. Feldman (2015).

The BAG3 Population: Potential for Orphan Designation



Source: Ziaeian and Fonarow 2016; Judge *et al.*, 2008; Hershberger *et al.*, 2010; Haas *et al.*, 2015; Knezevic *et al.*, 2015.

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Our Clinical Plan: AAV-*BAG3* Gene Therapies

Path with Decreased Risk to IND Filing and Initiation of Phase I/II Trial in DCM

Recent accomplishments provide a path with decreased risk to IND submission

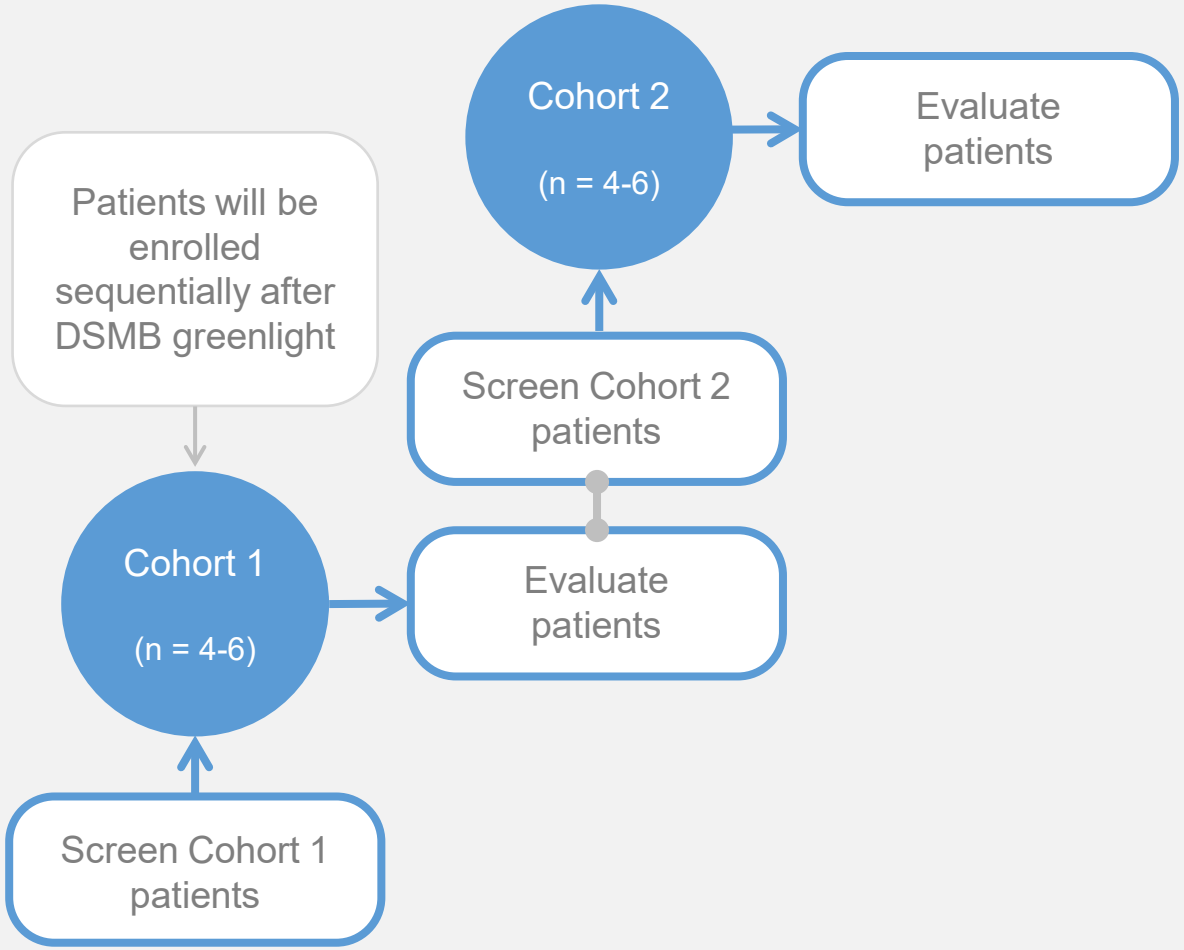
- **2016-2018:** Assess effect of BAG3 gene therapy in *in vivo* HF models across species (murine and porcine models)
- **2018:** Develop a BAG3 haploinsufficient DCM murine model to test BAG3 gene therapy efficacy
- **2018-2020:** Demonstrate REN-001 transduction efficiency, cardiac functional improvement in 5 models of heart failure (murine and porcine)
- **2020:** Complete pre-IND meeting with the FDA; confirm path to IND filing for phase I/II in DCM patients

Upcoming expected milestones include anticipated initiation of phase I/II trial in BAG3 DCM

- **Mid-2022. REN-001:** Anticipated submission of an IND in BAG3-associated dilated cardiomyopathy (DCM)
  - Complete dose ranging efficacy study in BAG3 haploinsufficient DCM murine model
  - Complete transduction efficiency and non-GLP toxicology profile of higher dose in normal Yucatan pigs
  - Get input from the FDA on phase I/II clinical protocol
  - Complete GLP toxicology and biodistribution study for IND filing (3-month endpoint)
- **Mid-2022. REN-001:** Anticipated initiation of phase I/II trial in DCM patients with BAG3 mutation (*BAG3*-associated DCM)

Proposed Phase I/II Clinical Study Design for REN-001

The planned study will enroll a total of 8-12 patients across two cohorts



Trial design:

- Multi-center, open-label, single-arm, dose escalation study in *BAG3*-associated DCM

Primary endpoint:

- Safety: Frequency and severity of AEs and SAEs
- Efficacy: Cardiac function by improvement in EF

Secondary endpoints:

- 6-minute walk test
- Kansas City Cardiomyopathy Questionnaire
- Serum biomarker (NT-proBNP)

Key inclusion criteria:

- Subjects aged 18-75 with left ventricle (LV) dysfunction
- Depressed LVEF as defined by AHA/ACC Guidelines
- NYHA Class II-III HF symptoms
- Elevated NT-proBNP
- Genetic variant in BAG3 consistent with haploinsufficiency and absence of other DCM causing variants as based on sequence analysis in a CLIA-certified laboratory

Value Proposition Highlights

- Developing single-dose REN-001 gene therapy candidate for familial DCM and other diseases due to *BAG3* mutation
- Compelling improvements in cardiac function demonstrated in multiple preclinical models
- Led by experienced management and exceptional cardiovascular disease and gene therapy scientific advisors
- IND submission and potential phase I/II trial initiation anticipated in mid-2022
- We believe BAG3 IP position provides important barriers to entry for significant market opportunity
- Backed by strong investor syndicate (experienced in CV and GT) that synergizes with CHAQ

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Thank You!

For follow-up please contact: info@renovacor.com

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Appendix

About Renovacor

BAG3 Gene Therapy Company Developing Precision Medicine for Diseases with High Unmet Need

Lead program: REN-001 GT for familial DCM with BAG3 mutations

- Treatment of monogenic cardiomyopathy (orphan BAG3 DCM)
- Rare disease with ~70,000 patients in US/EEA
- Preclinical data show improved cardiac function in multiple models
- Broad BAG3 IP position for BAG3 platform

Pipeline of proprietary gene therapies for BAG3-related diseases

- Heart failure (orphan and non-orphan)
- Neurodegenerative CNS diseases

Multiple Near- and Medium-term Expected Company Value Drivers

Near-term expected milestones (2021-2022)

- Path to IND expected to be agreed to with FDA
- Expected additional BAG3 gene therapy efficacy data in BAG3 haploinsufficient animal model
- Expected GLP tox and biodistribution data
- Expected IND submission for orphan BAG3 DCM

Medium-term expected milestones (2022-2023)

- Expect to start Phase I/II for orphan BAG3 DCM
- Option to expand lead program from intra-coronary dosing to also include IV dosing with immune modulation
- Anticipate second IND submission for follow-on indication

Significant Expertise and Strong Investor Syndicate

Leaders with deep domain expertise

- Highly experienced management team
- World renowned scientific founder (Arthur Feldman, MD, PhD) and scientific advisors in cardiovascular and gene therapy

Backed by strong investor syndicate

- Experienced biotech investors with deep domain expertise and track record of early investments in cardiovascular-directed therapies and AAV-based gene therapies

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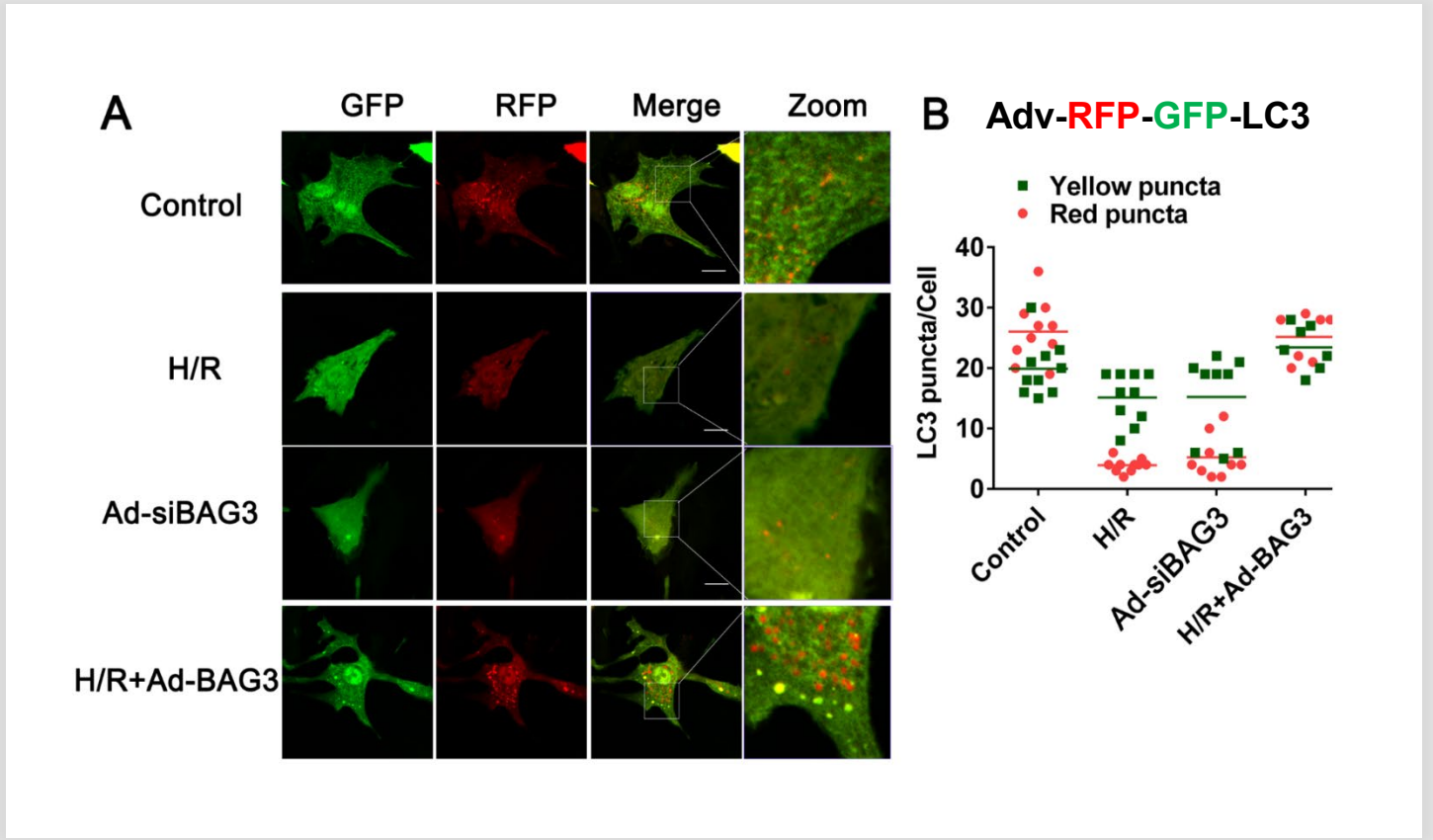
Preclinical Studies: The Mechanistic Rationale for Targeting BAG3 in Heart Failure

BAG3 in the Heart: Autophagy is Dependent on Levels of BAG3

Decreased autophagy flux is seen due to either: (1) hypoxia/re-oxygenation, H/R or (2) *BAG3* knock-down. Both have been shown to be reversed by addition of *BAG3* (Ad-*BAG3*)

Experiment

- Transfected neonatal mouse ventricular cardiomyocytes with autophagy reporter system then modulated BAG3 levels (using hypoxia/re-oxygenation (H/R) or BAG3 knock-down using BAG3 siRNA encapsulated in adenovirus (Ad-siBAG3)
- Yellow puncta = both RFP (red fluorescence) and GFP (green fluorescence) in autophagosomes
- Red puncta = quenched GFP from fusion of autophagosomes with lysosomes
- More yellow = less autophagy



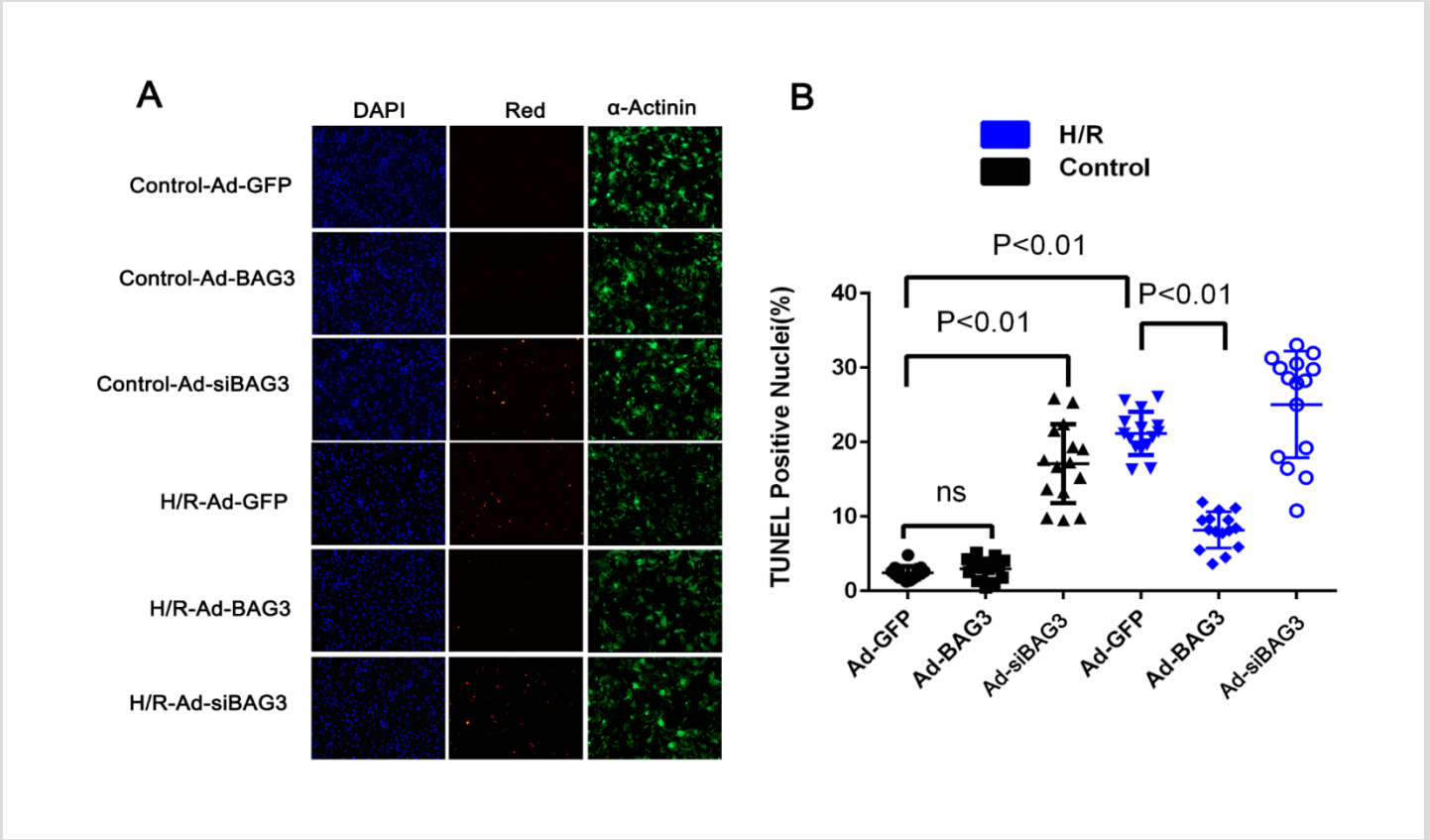
Source: Su F., ... Feldman, A.M., *JCI-Insight* 2016, 1, e90931; for dosing MOI = 8 [viral particles(1.6×10^7) ÷ number of cells(2×10^6)]

BAG3 in the Heart: Apoptosis is Dependent on Levels of BAG3

Increased apoptosis is seen due to either: (1) hypoxia/re-oxygenation, H/R or (2) *BAG3* knock-down. Both have been shown to be reversed by addition of *BAG3* (Ad-*BAG3*)

Experiment

- Transfected neonatal mouse ventricular cardiomyocytes with Ad-BAG3, GFP, or Ad-siBAG3 then exposed to H/R conditions
- Performed TUNEL assays identify apoptosis features
- Used a-actinin to identify cardiomyocytes
- Increase in TUNEL-positive nuclei is seen with low BAG3 levels and rescued with BAG3 expression

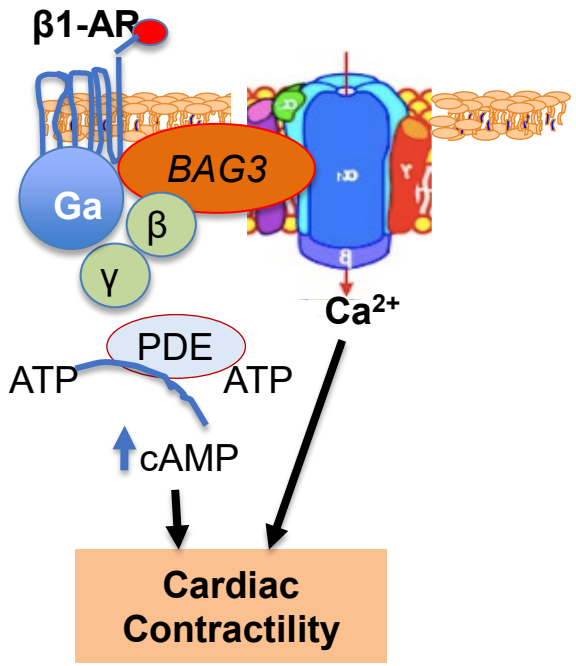


Source: Su F., ... Feldman, A.M., *JCI-Insight* 2016, 1, e90931; for dosing MOI = 8 [viral particles(1.6×10^7) ÷ number of cells(2×10^6)]

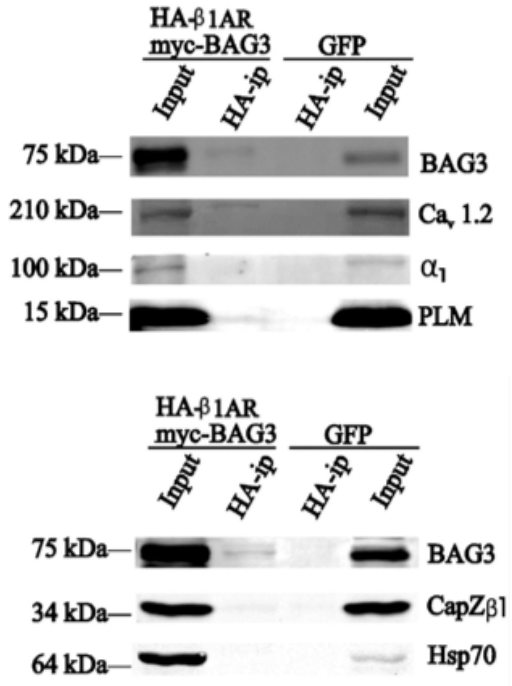
Association with β1-Adrenergic Receptor & L-Type Ca^{2+} Channel

BAG3 modulates heart muscle cell's contraction and action potential duration via interaction with the β-adrenergic receptor (b1-AR) and L-type Ca^{2+} channel

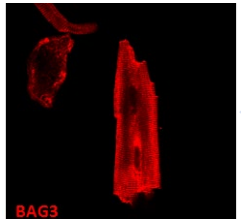
BAG3 modulates contractility



BAG3 associates with b1-AR

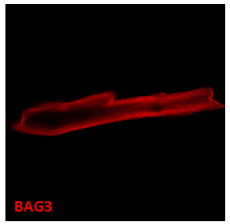


REN-001 restores BAG3



BAG3 is expressed control (red fluorescence)

BAG3 levels drop post-myocardial infarction (MI)

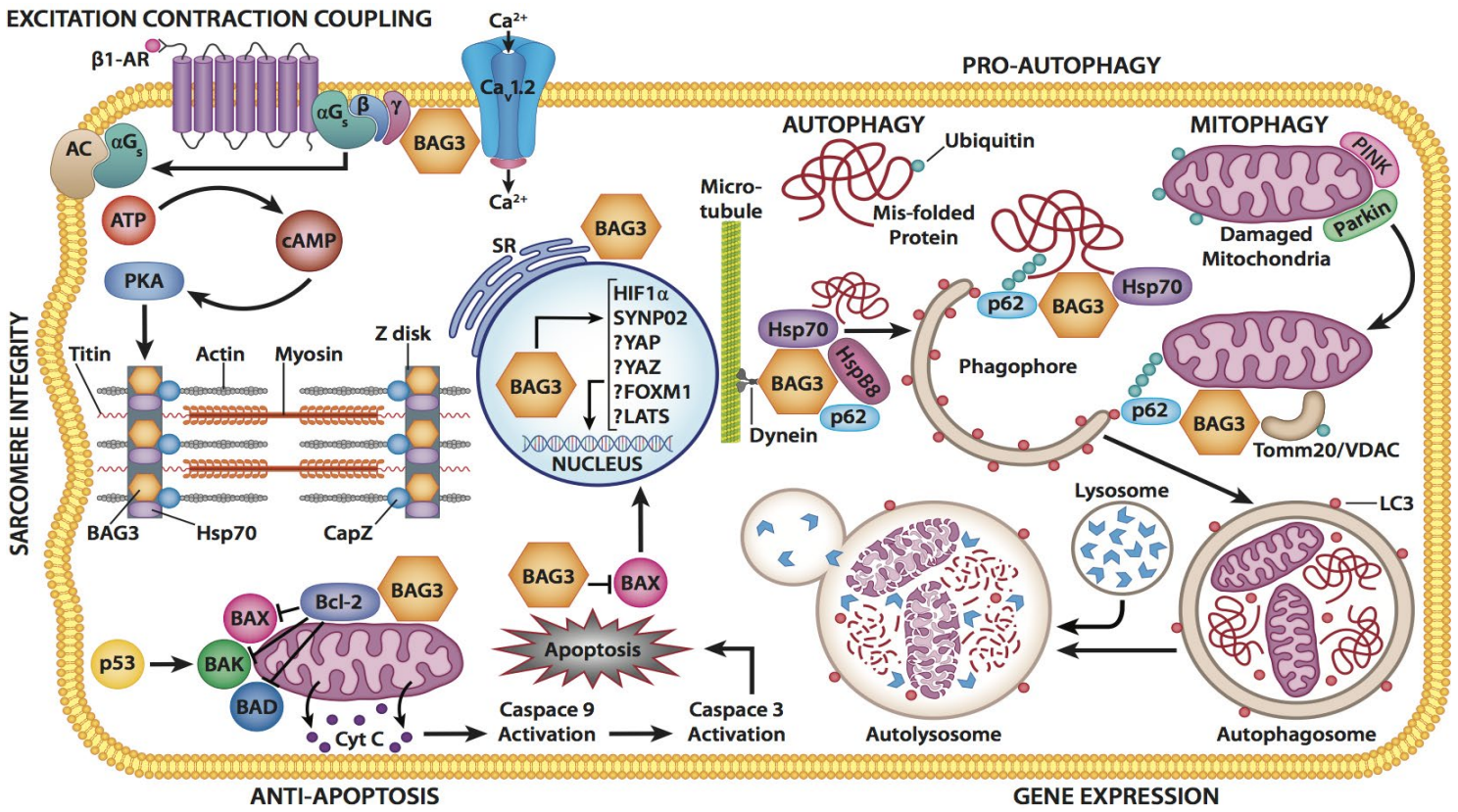


REN-001 rescues BAG3 expression post-MI

Source: Feldman, AM., *et al. J Mol Cell Cardiol.*, 2016, 92, 10-20

BAG3 Regulates Major Cell Pathways in the Heart

Normal cardiovascular function is dependent on right levels of BAG3 protein



Source: *Myers VD., … Feldman AM., J Am Coll Cardiol Basic Trans Science 2018;3:122–31*