Corporate Presentation

December 2021

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SEEKING GENE THERAPY CURES

NASDAQ: RCKT

Cautionary Statement Regarding Forward-Looking Statements

Various statements in this release concerning Rocket's future expectations, plans and prospects, including without limitation, Rocket's expectations regarding its guidance for 2021 in light of COVID-19, the safety, effectiveness and timing of product candidates that Rocket may develop, to treat Fanconi Anemia (FA), Leukocyte Adhesion Deficiency-I (LAD-I), Pyruvate Kinase Deficiency (PKD), Infantile Malignant Osteopetrosis (IMO) and Danon Disease, and the safety, effectiveness and timing of related pre-clinical studies and clinical trials, may constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995 and other federal securities laws and are subject to substantial risks, uncertainties and assumptions. You should not place reliance on these forward-looking statements, which often include words such as "believe," "expect," "anticipate," "intend," "plan," "will give," "estimate," "seek," "will," "may," "suggest" or similar terms, variations of such terms or the negative of those terms. Although Rocket believes that the expectations reflected in the forward-looking statements are reasonable, Rocket cannot guarantee such outcomes. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Rocket's ability to monitor the impact of COVID-19 on its business operations and take steps to ensure the safety of patients, families and employees, the interest from patients and families for participation in each of Rocket’s ongoing trials, our expectations regarding when clinical trial sites will resume normal business operations, our expectations regarding the delays and impact of COVID-19 on clinical sites, patient enrollment, trial timelines and data readouts, our expectations regarding our drug supply for our ongoing and anticipated trials, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials of its product candidates, Rocket's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Rocket’s Annual Report on Form 10-K for the year ended December 31, 2020, filed March 1, 2021 with the SEC. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and Rocket undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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Mission, Vision and Values

TRUST

Trust is given and trust is earned – it's a balance. The word trust comes from the Proto-Indo-European word deru which means "to be firm, solid, steadfast." Trust is the ground and foundation for everything we do.

GENEROSITY

Being generous means following up, sharing our best ideas, forgiving ourselves and others, asking who needs us, treating our word as gold, taking time to truly see others, and so many other things. The word generous has the same root as the word "gene" – which meant "to beget." Genes thrive on the generosity of others. What more is there to say?

CURIOSITY

The wonder of a child staring up at the night sky. Humility, egoless-ness. No single one of us can do this job alone and it is ok to ask for help. Curiosity is derived from the Latin word "cura" which gave birth to the word "care" as well as "cure." Generosity is to curiosity what gene is to cure.

ELEVATE

Derived from Latin levis which means "light" as opposed to heavy. How can we bring trust, generosity and curiosity to elevate ourselves, each other, the pipeline and ultimately the life experience of patients and their families?

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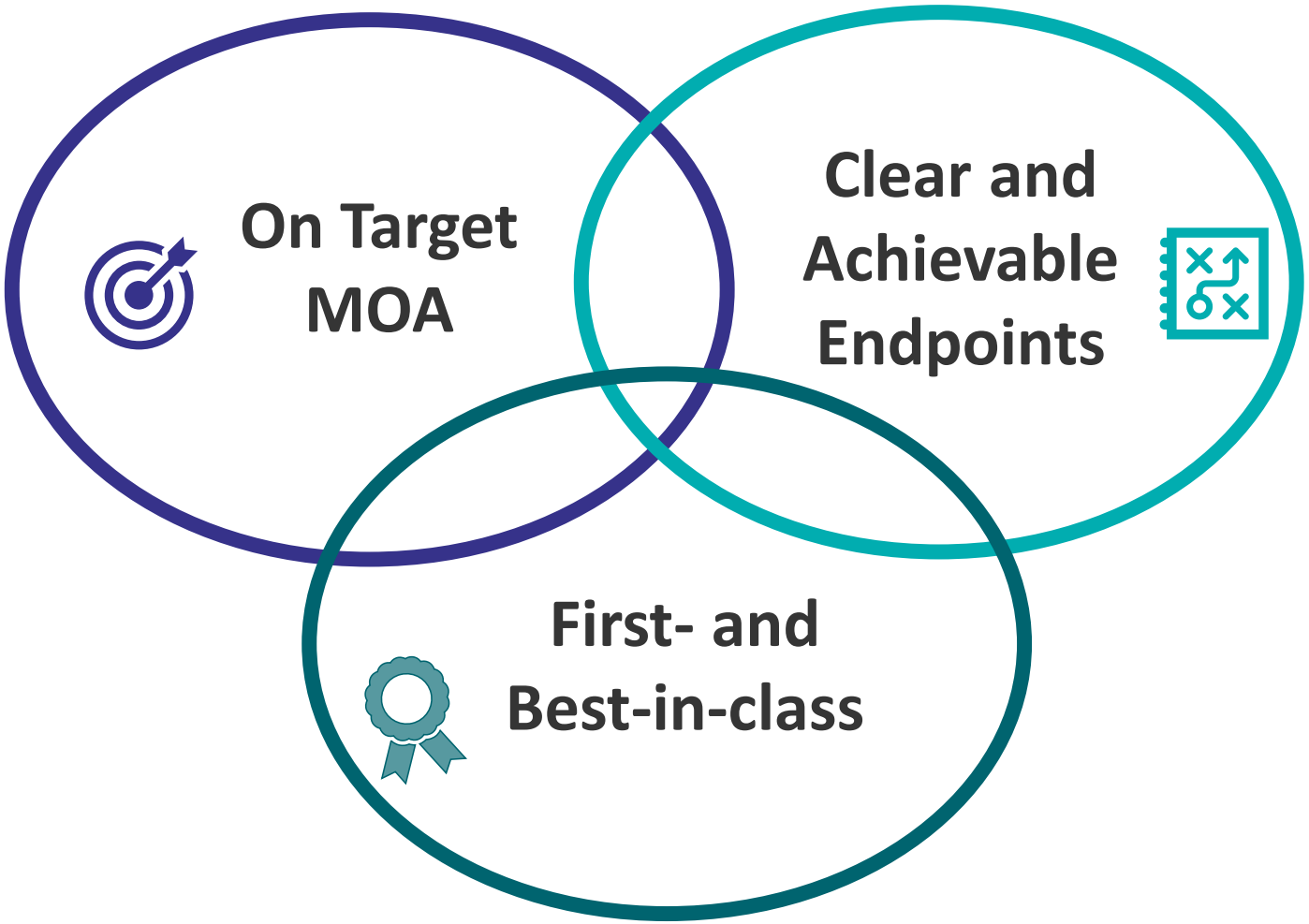
Multi-Platform Gene Therapy Targeting Rare Diseases



Focused on R&D Strategy for Sustainable Innovation

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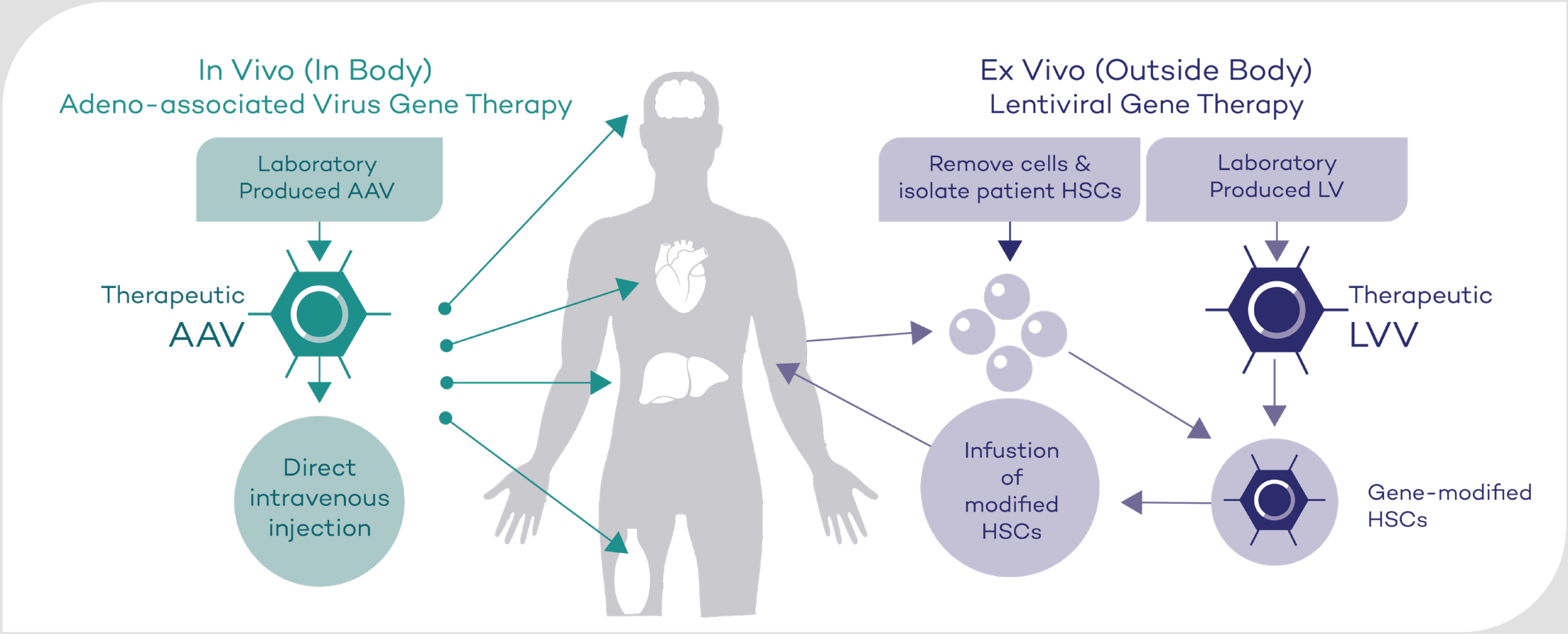
Gene Therapy: A Multi-Platform Approach



About Rocket Pharma

Multi-Platform Gene Therapy Company Targeting Rare Diseases: 1st-in-class with direct on-target mechanism of action and clearly-defined clinical endpoints

Ex-vivo Lentiviral vectors (LVV)

- Fanconi Anemia (FA)
- Leukocyte Adhesion Deficiency-I (LAD-I)
- Pyruvate Kinase Deficiency (PKD)
- Infantile Malignant Osteopetrosis (IMO)

In-vivo adeno-associated virus (AAV)

- Danon Disease

Multiple Near- & Medium-term Company Value Drivers

Near-term Milestones

- Additional Phase 1 data in Danon and PKD
- Potential registration-enabling dataset in FA and LAD-I
- In-house GMP manufacturing readiness

Medium-term Milestones

- First global submission (BLA)
- Platform establishment and pipeline expansion
- Current programs eligible for Pediatric Priority Review Vouchers

Strong Precedents and World-Class Expertise

Strong Precedents and Sound Strategy

- Compelling clinical proof-of-concept for LVV- & AAV-based therapies across a spectrum of genetic disorders
- Clearly-defined product metrics across indications
- Experienced company leadership
- Leading research and manufacturing partners

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Rocket's Leadership Team

Gaurav Shah, M.D.
Chief Executive Officer
Spearheaded Kymriah (CART-19) development at Novartis towards approval

Kinnari Patel, Pharm.D., MBA
President and Chief Operating Officer
Led Opdivo and six rare disease indication approvals

Raj Prabhakar, MBA
Chief Business Officer, SVP
~20 years cell, gene and biotech business development

Isabel Carmona, J.D.
Chief Human Resources Officer, SVP
Seasoned leader in human resources, legal and compliance across life sciences, financial services and IT

José Trevejo, M.D., Ph.D.
Chief Development Officer of AAV, SVP
~20 years of clinical development expertise

John Militello, CPA
VP, Principal Accounting Officer
~20 years public company finance and accounting experience, 6 years biotech experience

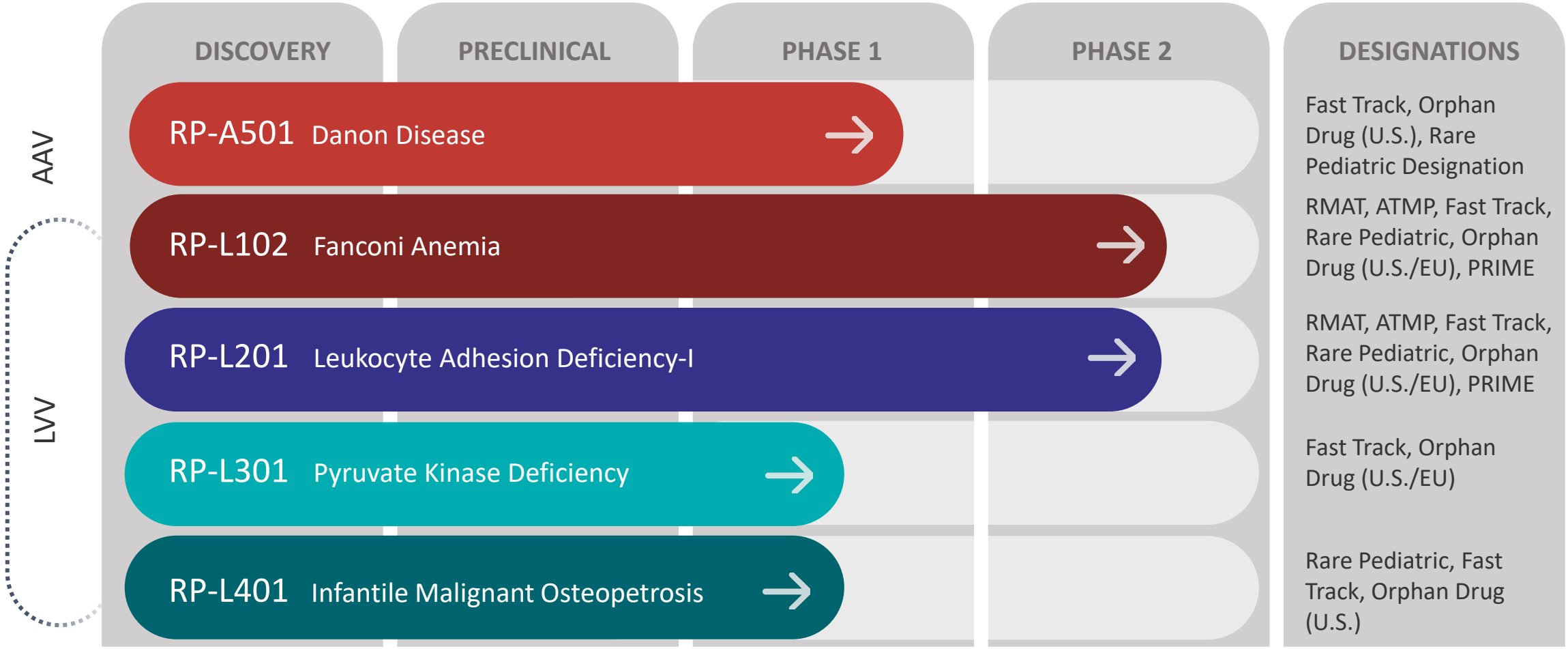
Jonathan Schwartz, M.D.
CMO & Clinical Development, SVP
Led multiple biologics approvals

Carlos Garcia-Parada, MBA
Chief Financial Officer
14 years of Oncology & Rare Disease experience
Leading role in launching Kymriah, the first CAR-T product on the market.

Gayatri R. Rao, M.D., J.D.
Chief Development Officer of LVV, SVP
7-Year Former Director of FDA's Office of Orphan Products Development

Ramji Krishnan, Ph.D.
VP, Manufacturing & Manufacturing Sciences
17+ years of CMC product development and life cycle management expertise

Rocket's Expanding Pipeline: Potential for Significant Value Creation Near and Long Term



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Fanconi Anemia (FA)
Monogenic DNA-repair disorder

RP-L102
Fanconi Anemia

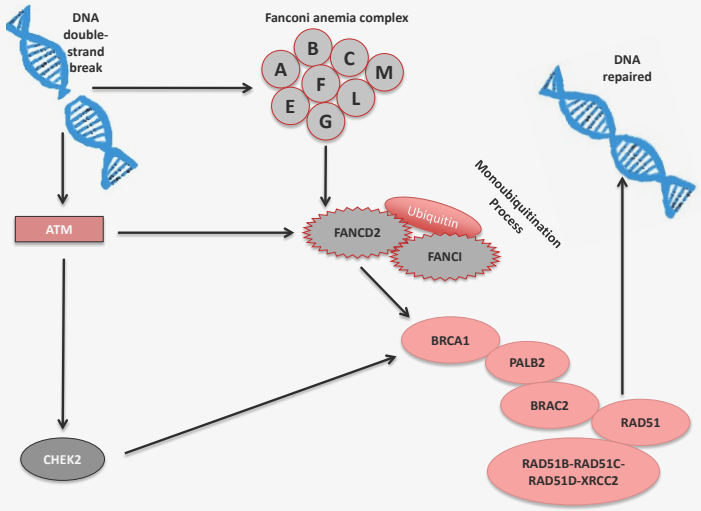
RP-A501
Danon Disease

RP-L201
Leukocyte Adhesion Deficiency-I

RP-L301
Pyruvate Kinase Deficiency

RP-L401
Infantile Malignant Osteopetrosis

OVERVIEW:



Bone Marrow

FANC-A Gene Mutation ⇨ Chromosomal breakage

- Platelets
- RBCs
- WBCs

Disease Sequelae:
- Birth Defects
- Skin Discoloration
- Developmental Issues

80% Bone Marrow Failure by Age 10
Acute Myeloid Leukemia
Head and Neck Cancer[1]
(↑ risk 30-50x)

Current available treatments: Allogeneic hematopoietic stem cell transplant associated with 100-day mortality, GVHD, and additional increased cancer risk

Addressable Market[2]: Estimated US + Europe target population of approximately 4,000 patients, 500 patients/year

RP-L102: LVV gene therapy that elicits phenotypic correction of blood cells and stabilization of previously declining blood counts

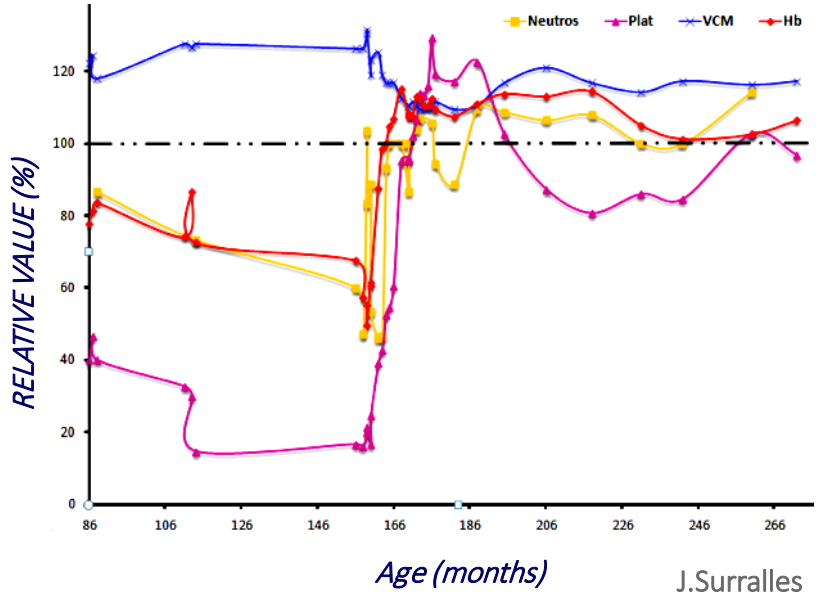
Regulatory Designations: Fast Track, Regenerative Medicine Advanced Therapy (RMAT) and Rare Pediatric Disease designations in the US; Advanced Therapy Medicinal Product (ATMP) classification and PRIority MEdicines (PRIME) in the EU; Orphan Drug designation in the US/EU

[1] Alter Br J Hametol 2010.
[2] 4,000 based on a detailed population analysis of FA genomic variants. 500 per year extrapolated by actual transplants per year plus patients from prevalence

Potential to Correct Bone Marrow Defect without Conditioning to Prevent Hematologic Failure

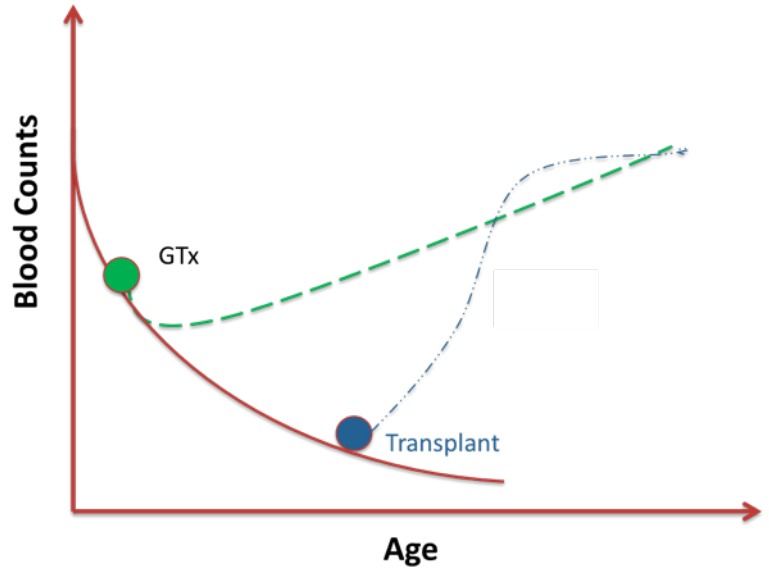
Rationale for GTx in FA:

- Somatic mosaicism demonstrates that a ***modest number*** of gene-corrected hematopoietic stem cells can repopulate a patient's blood and bone marrow with corrected (non-FA) cells.[1,2]



Gene Therapy Value Proposition:

- Potential to ***correct*** blood & bone marrow defect ***without conditioning***
- GTx implemented as preventative measure to ***avert bone marrow failure***; BMT is indicated for patients in whom marrow failure has occurred.



[1] Soulier, J., et al. (2005) Detection of somatic mosaicism and classification of Fanconi anemia patients by analysis of the FA/BRCA pathway. *Blood* 105: 1329-1336; [2]Data on file: Showing a single patient with a spontaneous correction of blood counts, no therapy administered.

FA Path to Product Registration

CIEMAT-Sponsored FANCOLEN 1 Study Process A

- Interim data (>12-month follow-up) showed evidence of durable engraftment, continued improvement in phenotypic markers and stabilization of previously-declining blood counts
- No conditioning required

OPTIMIZATION

Rocket-Sponsored Process B
(Optimized CD34 cell enrichment, transduction enhancers, commercial-grade vector and modified cell processing)

- Clinical trial of ~12 patients with sites at Stanford (US), Niño Jesús Hospital (Spain), and other leading centers in the US/Europe
- No conditioning required

BLA/ MAA

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RP-L102 “Process B”: Pivotal Clinical Trials and Outcome Measures

RP-L102 Studies	Non-randomized, open label studies: US Phase 1, US Phase 2, and EU Phase 2 (FANCOLEN-II)	
CMC/Drug Product	**“Process B”** includes cell enrichment, transduction enhancers, commercial-grade vector and modified cell processing	
Inclusion Criteria	Focus on patients with no/limited marrow failure, optimize preventative potential in absence of conditioning Minimum age: 1; Maximum age: US Ph 1 (12-yrs); US Ph 2 (none); EU Ph 2 (17-yrs) BM CD34+ concentration ≥ 30/µL (from aspirate); if BM CD34+ of 10-29/µL, then at least 2 of the following: Hb ≥ 11g/dL, ANC ≥ 900/µL, or Platelets ≥ 60,000/µL US Ph 1 only: At least 1 hematologic parameter (Hb, ANC or Plt) below lower limit of normal	
Exclusion Criteria	Available & eligible HLA-identical sibling donor MDS or leukemia (including associated cytogenetic abnormalities) Mosaicism with stable/improved blood counts	
Endpoints	**Efficacy**	**Engraftment**: Peripheral blood (PB) and BM vector copy number (VCN) **Phenotypic correction**: Increased resistance of BM and PB cells to MMC and DEB **Clinical response**: Prevention of BMF
	Efficacy in 5 of 12 patients (defined as >10% MMC resistance at two time points observed between 12-36m post rx) required to reject null hypothesis	
	Safety of RP-L102	

Post rx = Post-treatment

RP-L102 Treated Study Patients

Phase	Subject #	Site	Age at Enrollment	Gender	Follow-up
PHASE 1	1 (1001)	US	5	F	32M
	2 (1002)*	US	6	F	18M*
PHASE 2	3 (2004)	Spain	3	M	21M
	4 (2008)	Spain	2	F	15M
	5 (2009)	Spain	3	M	15M
	6 (2010)	US	3	M	15M
	7 (2011)	US	5	F	15M
	8 (2014)	UK	6	F	12M
	9 (2016)	US	2	M	9M
	10 (2021)	UK	2	F	~2M†
	11 (2023)	UK	5	F	0M‡

- 11 subjects treated across 3 clinical sites, 2 under US Phase 1 and 9 under global Phase 2
- All subjects ≤6 years at enrollment
- 8 subjects have ≥12 months of follow-up; 1 subject withdrawn from the study; 3 remaining subjects treated more recently with more limited follow-up
- Note: Follow-up has been challenged by COVID-19 pandemic

** Subject withdrawn from the study at 18 months post-RP-L102 infusion; received successful allogeneic HSCT*
† Subject recently received RP-L102 infusion as of October 2021
‡ Subject recently received RP-L102 infusion as of December 2021

RP-L102 Investigational Product Metrics

Phase	Subject #	CD34+ Cells/kg	CFCs/kg	Mean VCN: Liquid Culture	Mean VCN: CFCs	Transduction Efficiency (%)	CFC Survival MMC 10nM (%)
PHASE 1	1 (1001)*	2.0×10^5	5.2×10^4	2.08	0.62	67	33
	2 (1002)*	3.7×10^5	5.0×10^4	2.21	0.92**	72	47
PHASE 2	3 (2004)	4.8×10^5	1.1×10^5	1.70	0.73	100	63
	4 (2008)	3.2×10^6	2.8×10^5	1.65	1.56	97	63
	5 (2009)	1.9×10^6	1.5×10^5	2.16	0.76	61	45
	6 (2010)*	4.1×10^6	n/a	0.62	n/a	n/a	n/a
	7 (2011)*	2.8×10^6	n/a	1.46	n/a	n/a	n/a
	8 (2014)*	5.4×10^5	3.6×10^4	3.68	pending	pending	31
	9 (2016)*	3.0×10^5	2.5×10^4	1.96	0.64	88	64
	10 (2021)*†	2.3×10^6	pending	pending	pending	pending	pending
	11 (2023)*‡	2.5×10^5	pending	pending	pending	pending	pending

Overall DP metrics are consistent with the more optimally treated subjects from FANCOLEN-I study

<u>Mean values</u>:
VCN (liq) 1.95
VCN (CFC) 0.87
TD efficiency 81%
CFC MMC-res 49%

Overall transduction and MMC-resistance levels in DP are consistent with high degree of corrected HSPCs

*Per NC200 automated count (results in ~50% lower count vs. manual used in FANCOLEN-I).

**Mean CFC VCN was assessed from a cryopreserved drug product sample.

Data as of December 2021. "Optimally" means of the nine patients treated in Fancolen-I the two that had the best benefit risk

† Subject recently received RP-L102 infusion as of October 2021
‡ Subject recently received RP-L102 infusion as of December 2021

CFCs: colony forming cells
VCN: vector copy number
MMC: mitomycin-C

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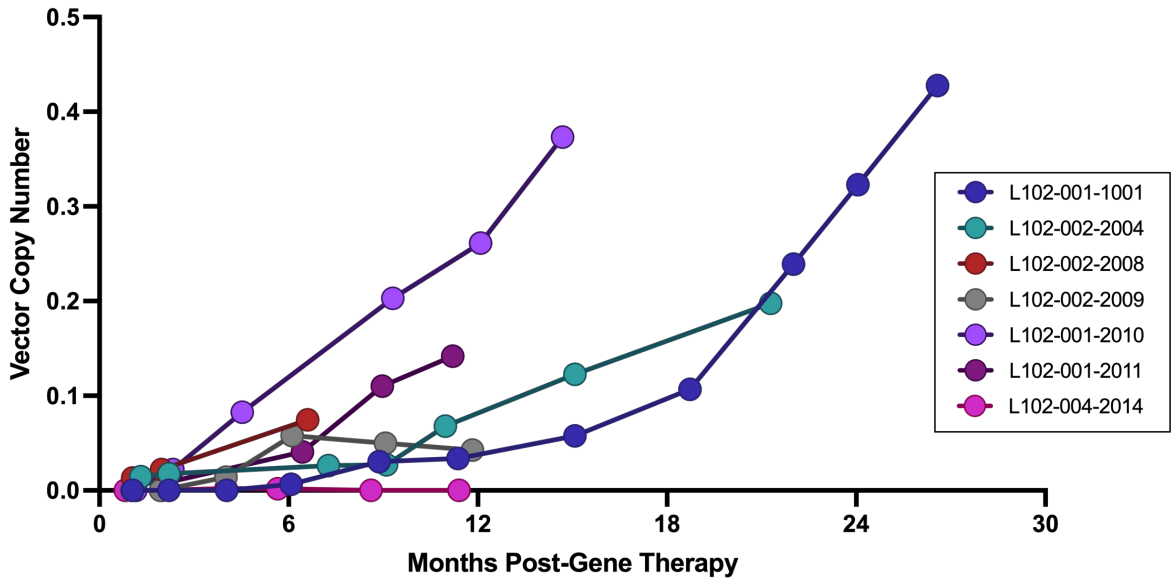
RP-L102 Study Patients with ≥12m Follow Up Demonstrate Evidence of Genetic and Phenotypic Correction



- **Sustained PB VCN in 6 of 7 currently enrolled patients with ≥ 12 months of follow up**
- **Concomitant BM CFC MMC resistance ≥ 10% above baseline values**

NOTE: Efficacy (defined as MMC resistance ≥ 10% at two or more timepoints) in 5 of 12 patients required to reject null hypothesis.

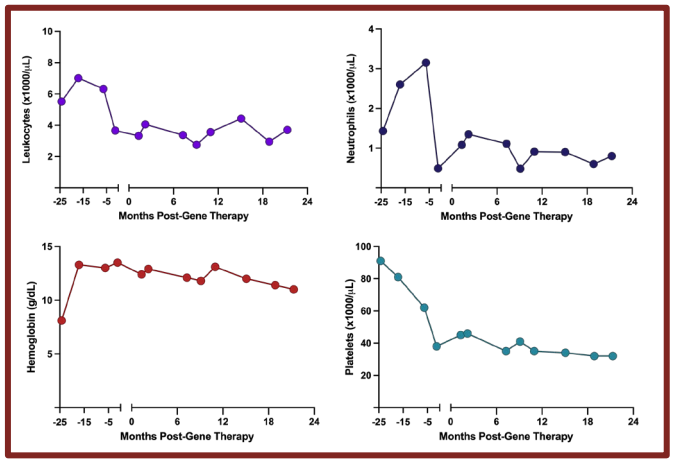
Subject #	Patient Age at Treatment	Bone Marrow Assessment Performed (months)	BM CFC MMC Resistance at 10 nM MMC (%)
1 (1001)	5	24	16†
3 (2004)	3	21	63
4 (2008)	2	12	21
5 (2009)	3	12	29
6 (2010)	3	12	42
7 (2011)	5	12	31
8 (2014)	6	12	0

† Assessment was not performed at study's centralized laboratories

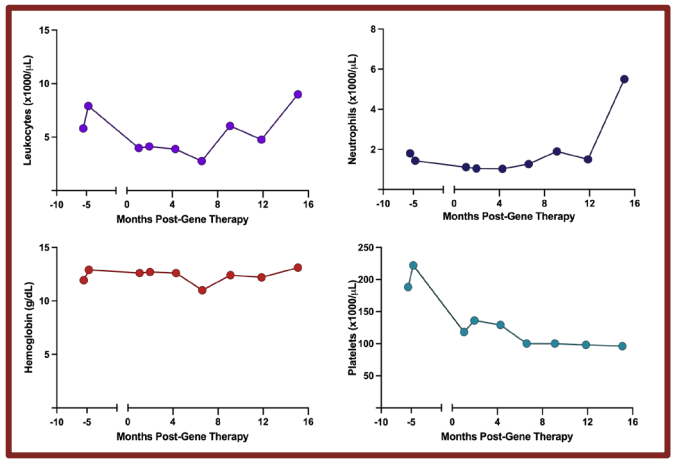
Data as of December 2021

Blood Count Stabilization in at Least 5 Patients with BM CFC MMC Resistance ≥10%

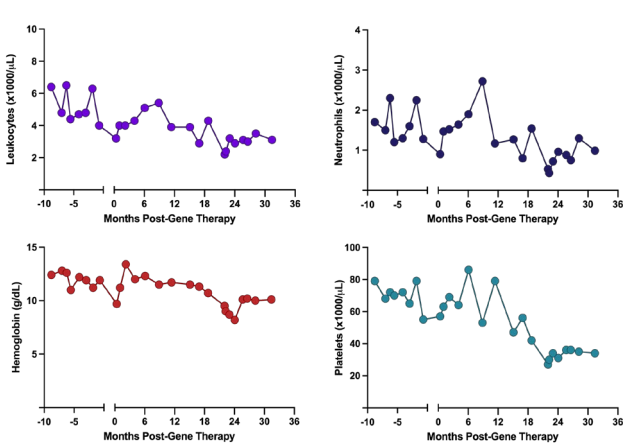
Subject 3 (2004)



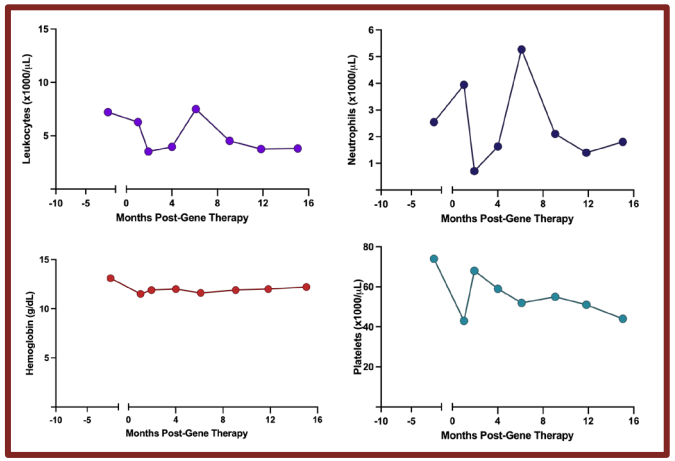
Subject 4 (2008)



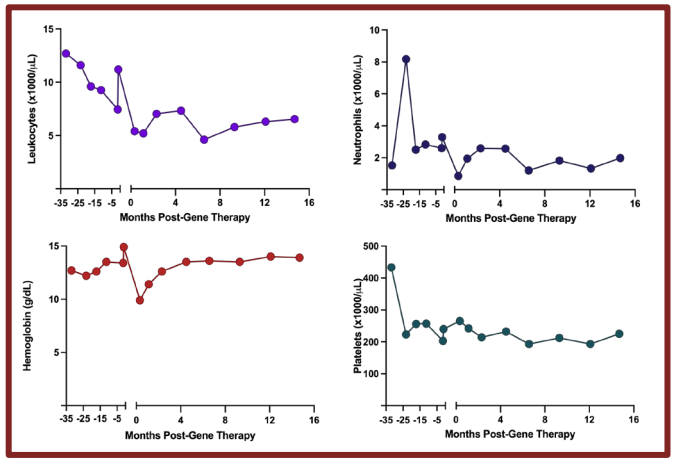
Subject 1 (1001)



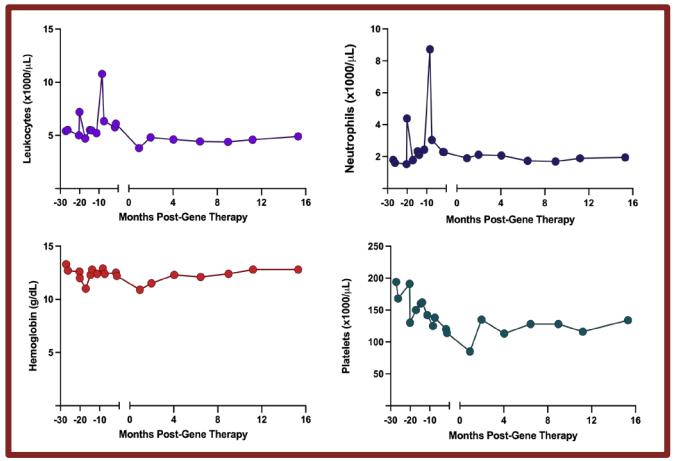
Subject 5 (2009)



Subject 6 (2010)



Subject 7 (2011)



- **Blood count stabilization in 5/5 patients with BM CFC MMC Resistance ≥ 20%**
- **Patient 1 (1001; MMC-res 16%) had modest decline in blood counts with potential stabilization after ~18m; no transfusions have been required**

Data as of December 2021

Summary of Pivotal RP-L102 Treated Study Patients

11 Patients have received RP-L102

7 of 9 showed preliminary evidence of engraftment

N = 8 with ≥ 12M Follow-up (12-32M)

- **6 of 8** showed increasing evidence of engraftment with increase in MMC resistance ranging from **16-63%**
- 1 patient's course (1002) complicated by *Influenza B* infection; required BMT

N = 3 with < 12 months of follow-up

- All patients clinically stable post-treatment; the patient who required BMT underwent transplant at 18-months and engrafted without complications
- RP-L102 related SAEs: 1 transient infusion-related reaction (Grade 2)
- Patient enrollment and follow-up has been challenged by COVID-19 pandemic

Data as of December 2021

RP-L102 Conclusions: Optimized "Process B" Appears to be a Consistent and Reproducible Improvement over "Process A"

- ***11 patients treated*** with "Process B"
- Safety results appear ***highly favorable***
  - Patients treated without conditioning
  - No signs of dysplasia or other concerning features
  - RP-L102 related SAEs: 1 transient infusion-related reaction (Grade 2)
- Increasing evidence of ***engraftment*** observed in ***6 out of 8 patients followed for 12 months or longer***
  - 1 patient's course complicated by Influenza B resulting in progressing BMF; successfully received BMT at 18-months
  - Increasing BM CFC MMC-resistance (range from 16-63%) seen in 6 subjects at minimum of one timepoint*

** Efficacy in 5 of 12 patients (defined as >10% MMC resistance at two time points observed between 12-36m post rx) required to reject null hypothesis*

Data as of December 2021

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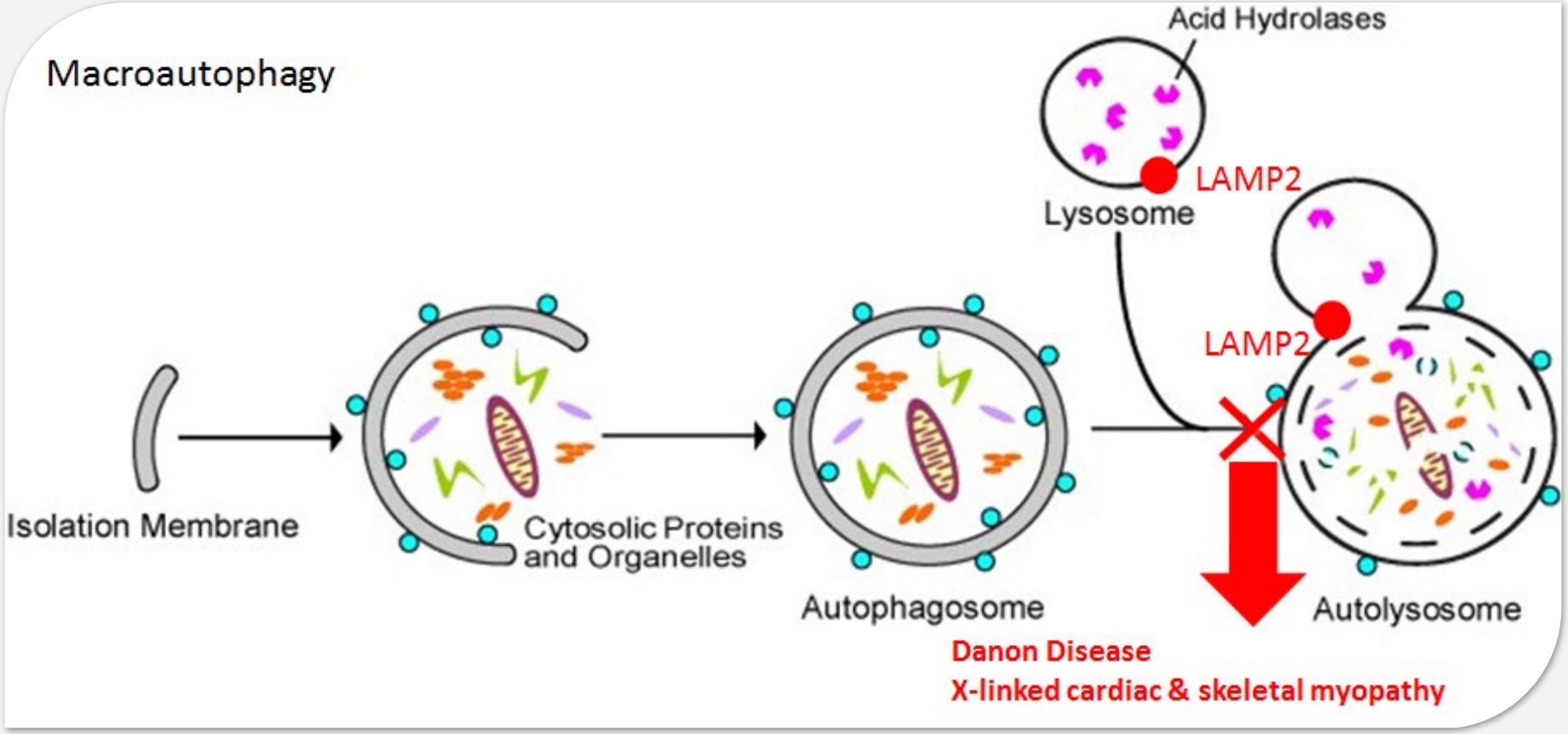
Danon Disease
Monogenic Heart Failure Syndrome

RP-L102	**RP-A501**	RP-L201	RP-L301	RP-L401
Fanconi Anemia	Danon Disease	Leukocyte Adhesion Deficiency-I	Pyruvate Kinase Deficiency	Infantile Malignant Osteopetrosis

OVERVIEW:

- **Background:** *Devastating* ***multisystemic disorder*** caused by highly penetrant and X-linked dominant ***LAMP2 mutations***, rapidly progressive cardiomyopathy is predominant cause of morbidity and early mortality in adolescents & young adults
- **Currently available treatments**: *Non-curative* heart transplants associated with considerable morbidity and mortality
- **Addressable Market:** Estimated US + Europe prevalence of ***15,000-30,000***
- **RP-A501**: AAV9 gene therapy product that elicits *improvements* in *survival*, cardiac function, and liver enzymes in preclinical studies
- **Regulatory Designations**: Orphan Drug, Rare Pediatric & Fast Track designations in the US

An Impairment in Autophagy Caused by *LAMP2B* Mutations



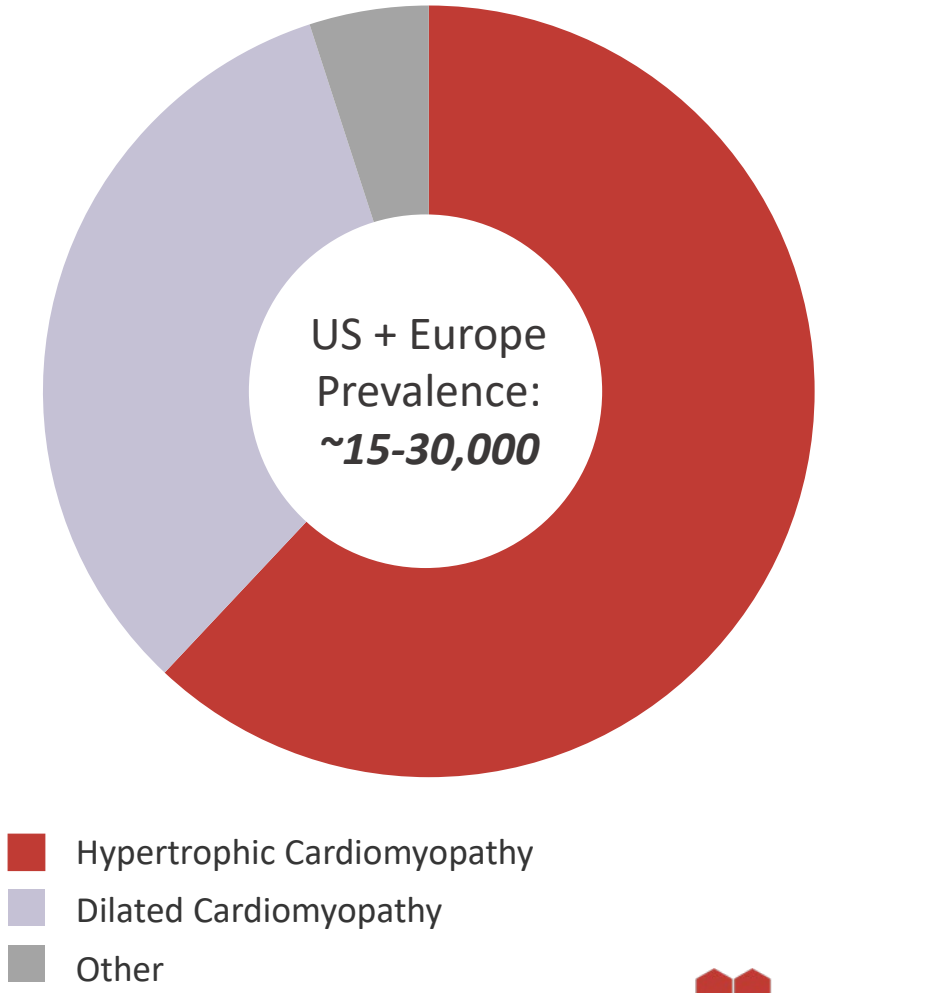
Epidemiology and Market Opportunity

Hypertrophic Cardiomyopathy (HCM)

- US HCM Prevalence: 600K-1MM+*
- 1-4% of HCM patients consistently identified with LAMP2 mutations in multiple studies with >1000 subjects evaluated**
- Danon Disease Patients with HCM: ***
  - 85% of males
  - 30% of females

Dilated Cardiomyopathy (DCM)

- Danon Disease Patients with DCM ***
  - 15% of males
  - 50% of females



* J Am Coll Cardiol. 2015 Mar 31;65(12):1249-1254.
** Heart. 2004 Aug;90(8):842-6. N Engl J Med. 2005 Jan 27;352(4):362-72. Genet Med. 2015 Nov;17(11):880-8. Gene. 2016 Feb 15;577(2):227-35. J Cardiovasc Transl Res. 2017 Feb;10(1):35-46
*** Neurology. 2002 Jun 25;58(12):1773-8. Genet Med. 2011 Jun;13(6):563-8. Rev Esp Cardiol (Engl Ed). 2018 Aug 11.

Danon Disease Causes 1-4% of Hypertrophic Cardiomyopathy:
Consistent Presence in Multiple Series Published 2004-Present

Author & Year	Age	n HCM	n Danon	% Danon	Note
Charron 2004	N.A.	197	2	1.0%	Studied LAMP2 mutations in 197 HCM patients at a general hospital in Paris
Arad 2005	12-75	75	2	2.7%	Studied glycogen storage diseases in 75 consecutive pts diagnosed with HCM (multicenter US/EU). No cases of Pompe or Fabry were detected.
Yang 2005	1m-15y	50	2	4.0%	Studied LAMP2 mutations in 50 pts with ped./juvenile onset HCM (single US center). Additional DD identified in relatives of the n=2 probands were not included in this analysis.
Cheng 2012	N.A.	50	3	2.3%	Studied LAMP2 mutations in 50 consecutive pts diagnosed with concentric LVH at a general hospital in Peking. (Concentric LVH is seen in appx. 38% of HCM). DD incidence higher (3/36) when n=14 w/ cardiac amyloidosis were removed from n=50 cohort.

Charon et al. Heart 2004; 90:842-6.
Arad et al. N Engl J Med 2005; 352;362-72.
Yang et al. Circulation 2005; 112:1612-17.
Cheng et al. Eur Heart J 2012; 33:649-56.

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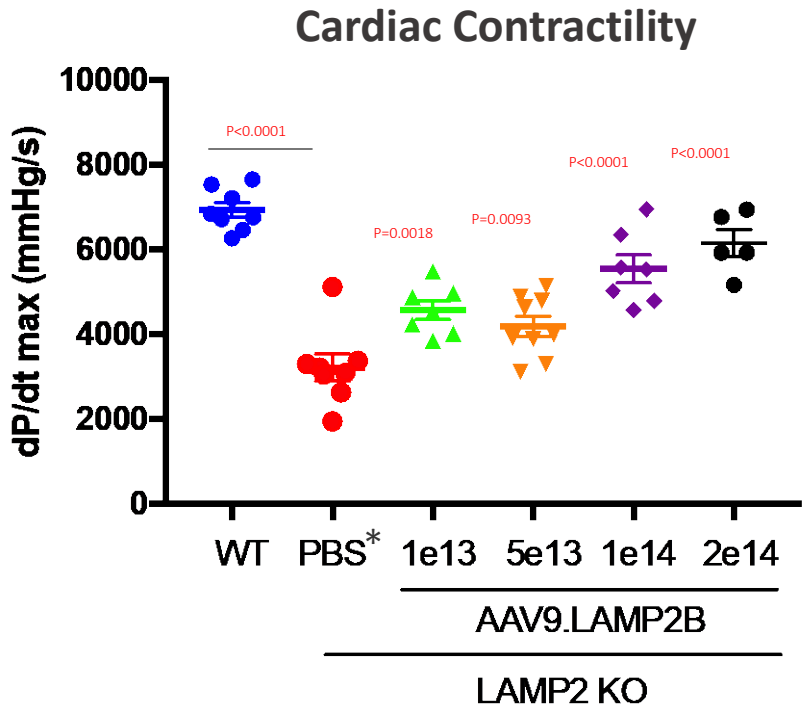
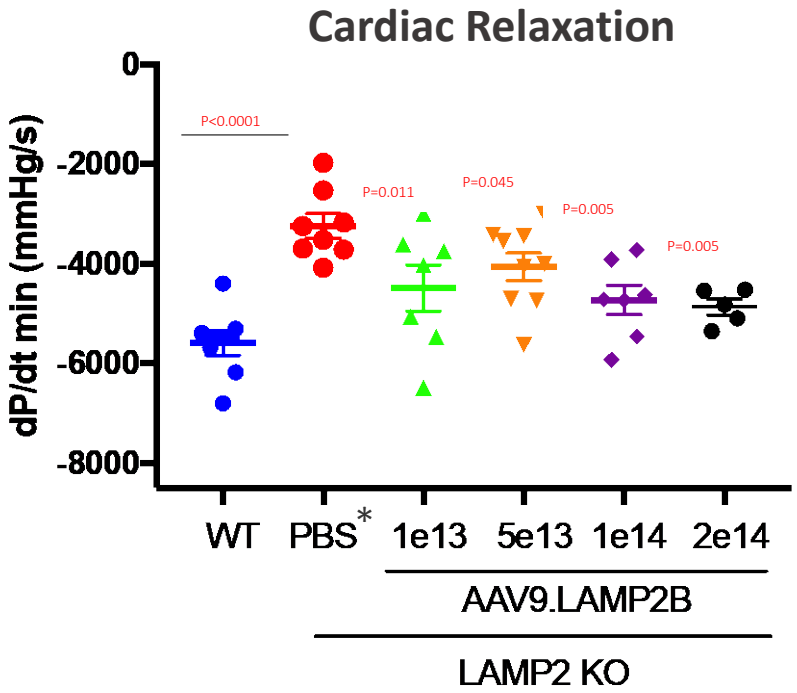
RP-A501 Restores Cardiac Function in KO Mice

Dose-Dependent Improvements in Systolic and Diastolic Function in LAMP2 KO Mice

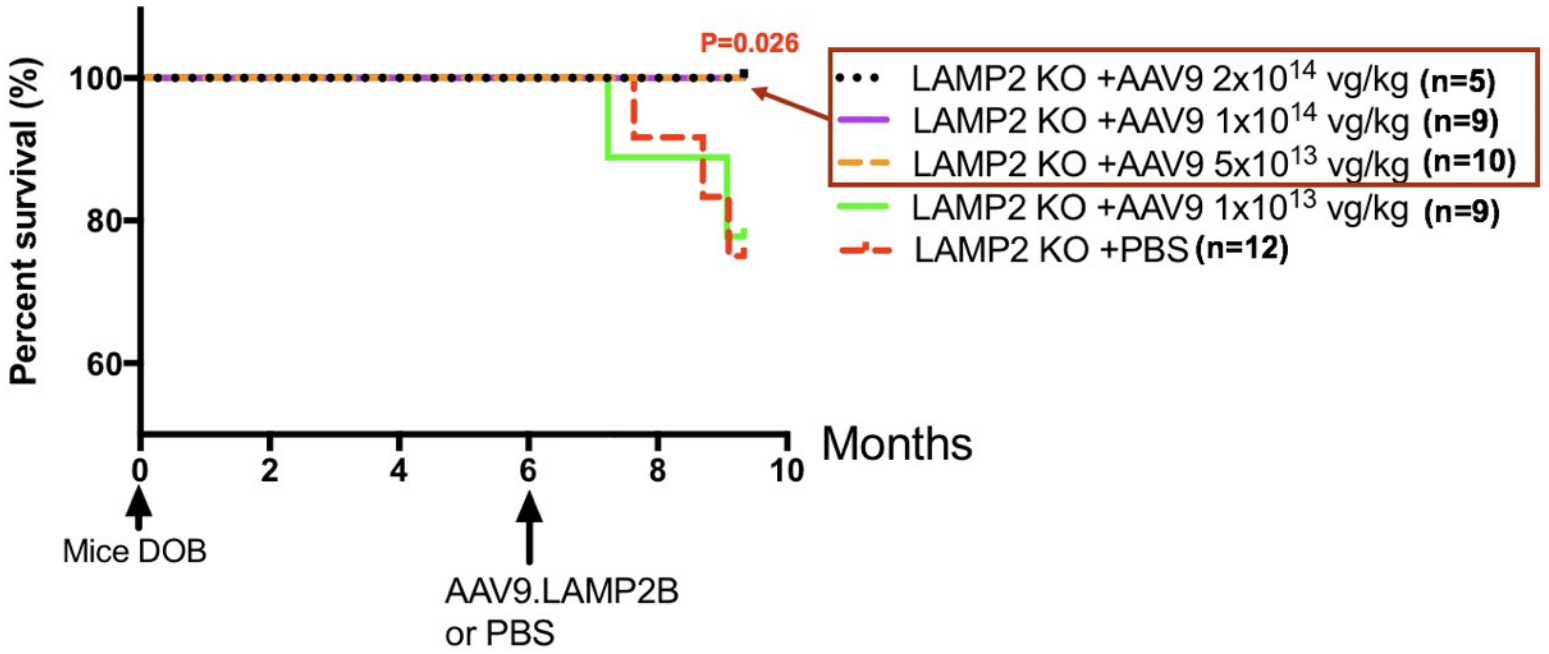




Lower dP/dt max indicates impaired contractility; Higher (less negative) dP/dt min indicates impaired heart relaxation

*PBS = Phosphate Buffered Saline (Negative Control)

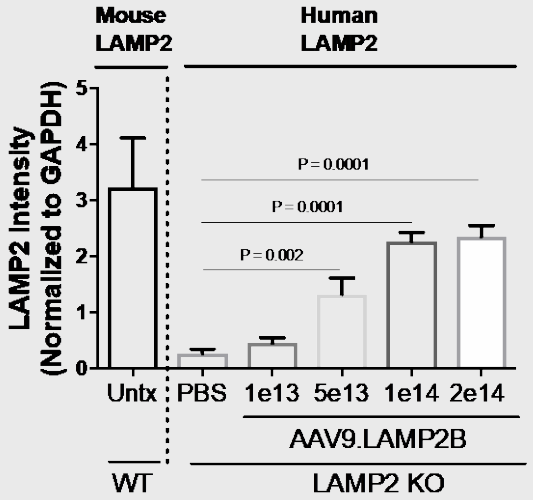
RP-A501 Shows Survival Benefit at Higher Doses in Preclinical Studies



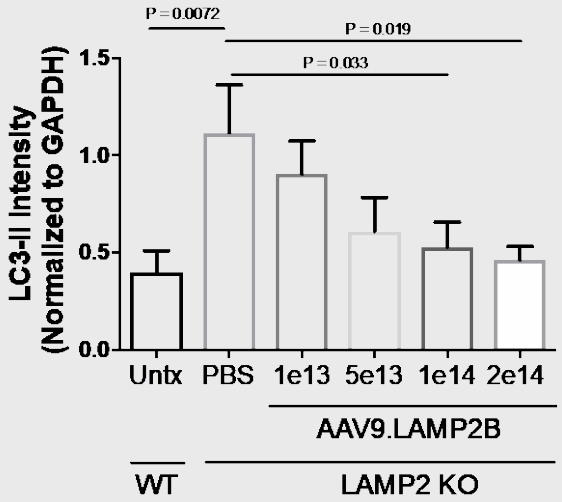
Note: All mice were sacrificed at Month 10

Protein: RP-A501 Elicits Durable Expression of LAMP2B Protein and Autophagy in Heart[1]

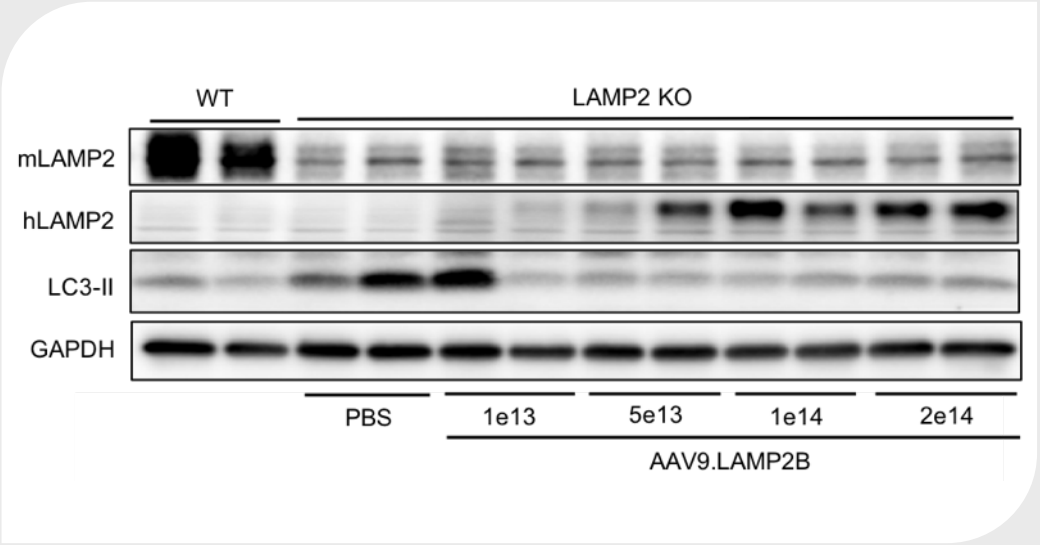
LAMP2 PROTEIN EXPRESSION



LC3-II PROTEIN EXPRESSION

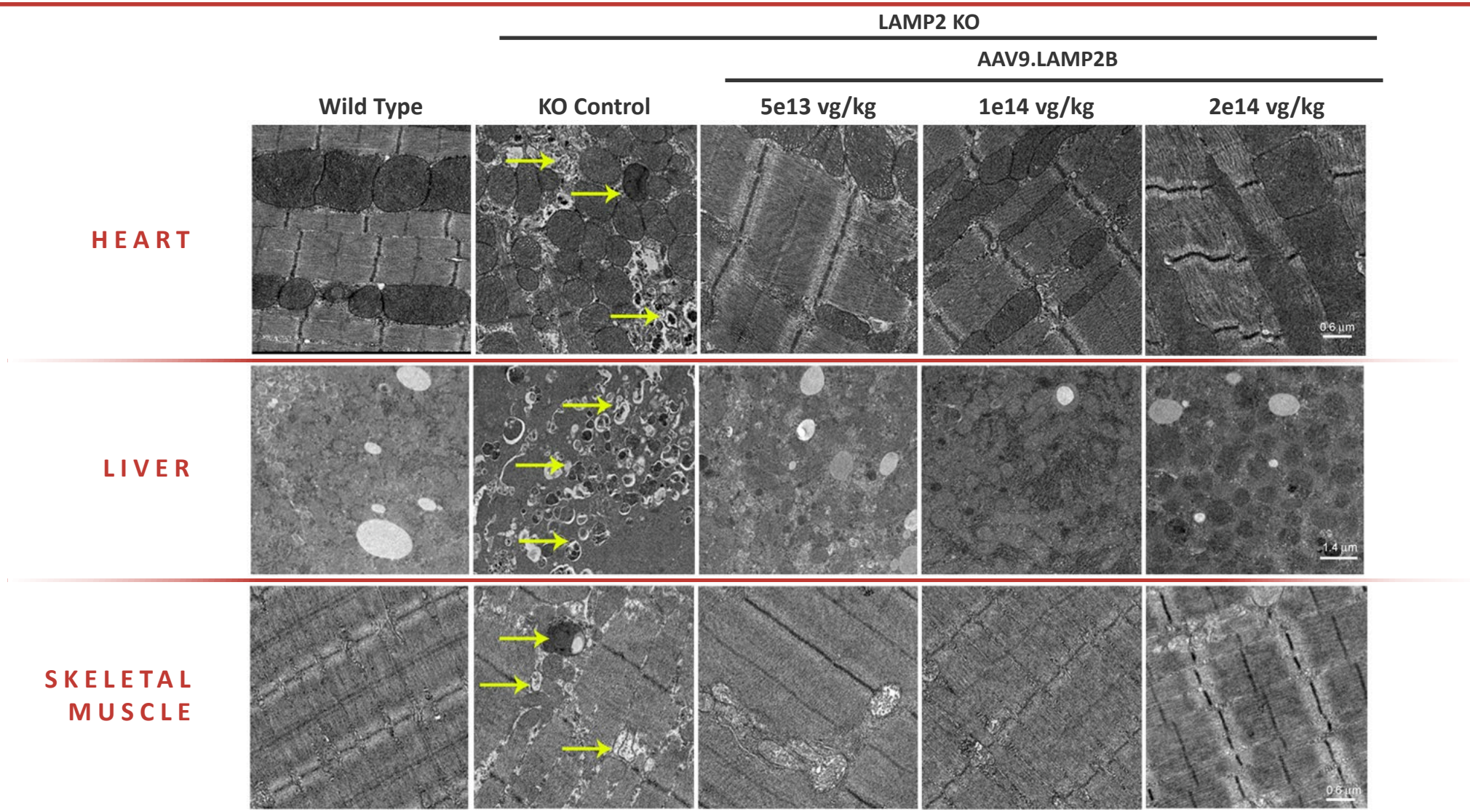


WESTERN BLOT

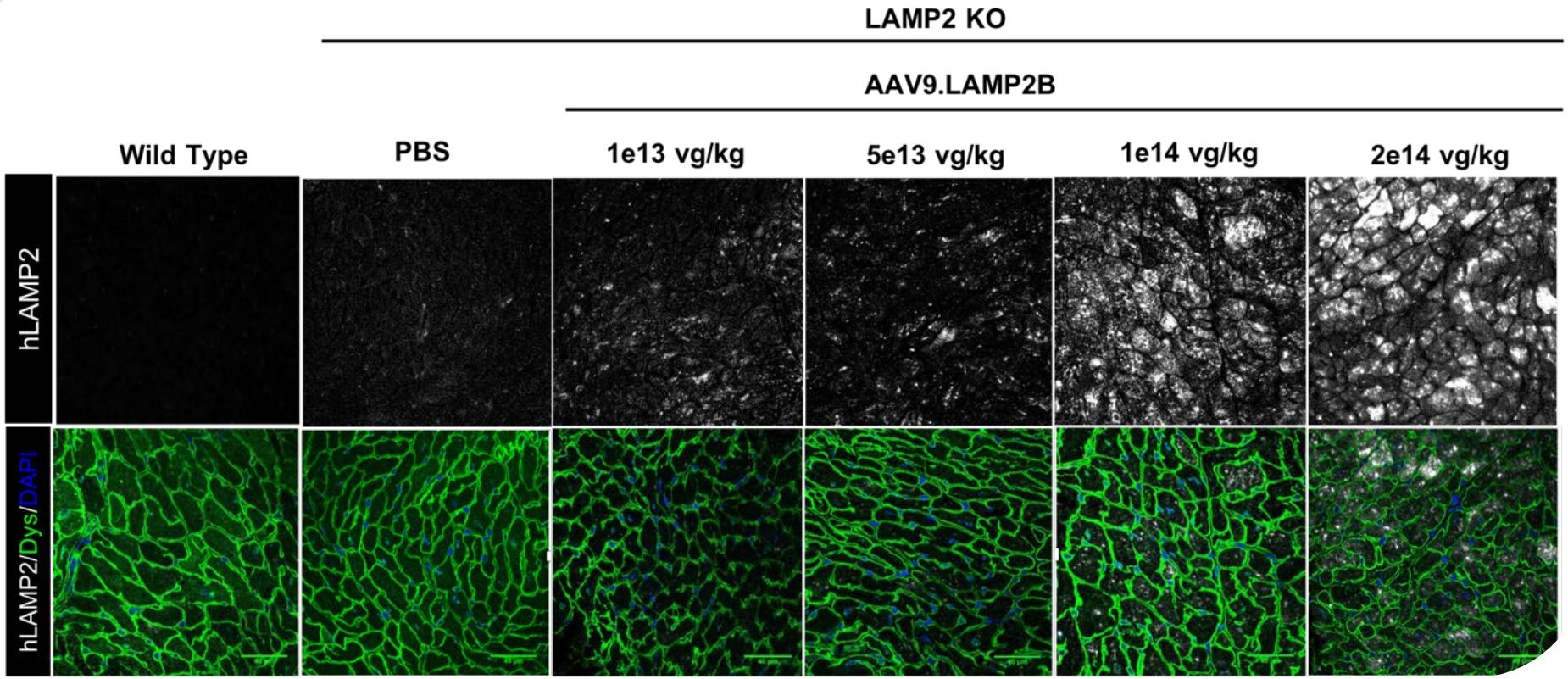


[1]Data are Mean ± SEM. N=5-8 per group. Untx = Untreated, PBS = Phosphate buffered saline
Note: Mouse LAMP2 and Human LAMP2 data are from separate Western blots.

Structural: RP-A501 Reduces Autophagic Vacuoles in All KO Mouse Models



Dose-dependent LAMP2 Expression in Cardiac Tissue



AAV9 Vector Shows Consistent Cardiac Tropism in Several Studies Across Different Species

DISORDER & VECTOR	DOSE	SPECIES	RESULTS	SPONSOR	REFERENCE
LGMD2A AAV9.hCAPN3	3E+13 vg/kg	NHP	8-80-fold higher transduction in cardiac vs. skeletal muscle	Genethon	Lostal (ASGCT 2018)
Non-specific AAV9.Luc	3E+12 vg/kg	NHP	~ 10-fold higher transduction in cardiac vs. diaphragm; and comparable to other muscle	UNC	Tarantal 2016
Pompe AAV9.hGAA	1E+11 vg/mouse	Mouse	~ 10-fold higher transduction in cardiac vs. diaphragm	U. Florida	Falk 2015
DMD AAV9.mDys	1.9 - 6.2E+14 vg/kg	Dog	2-3 fold higher transduction in cardiac vs. skeletal muscle	U. Missouri	Yue 2015
SMA AAV9.SMN	3E+14 vg/kg & 1E+13 vg/kg	Mouse & NHP	~ 100-fold higher transduction in cardiac vs. skeletal muscle (mouse)	Nationwide Children's	Meyer 2014
MPSIIIB AAV9.hNAGLU	1 - 2E+13 vg/kg	NHP	≥ 10-fold higher transduction in cardiac vs. skeletal muscle in majority of animals	Nationwide Children's	Murrey 2014
Non-specific AAV9.Luc	5E+10 vg/mouse	Mouse	5-10-fold higher transduction in cardiac vs. skeletal muscle	UNC	Pulicherla 2011
Pompe AAV9.hGAA	4E+05 - 4E+08 vg/mouse	Mouse	~ 8-12-fold higher transduction in cardiac vs. skeletal muscle or diaphragm	U. Florida	Pacak 2006
SMA AAV9.SMN	2E14 vg/kg	Human	Heart VCN ~3-4, Muscle & CNS ~1	AveXis	Kaspar 2019 (ASGCT 2019)

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Summary of Preclinical Data

- **Shows Phenotypic Improvements at Low-Dose 5e13 vg/kg:**
  - ***Survival*** benefit at higher doses
  - Dose-dependent ***restoration*** of cardiac function
  - Improvement in transaminases
- **RP-A501 *Reduces* Autophagic Vacuoles in All Examined Organs: Heart, Liver, Skeletal Muscle**
- **RP-A501 Elicits *dose-dependent increase* in LAMP2 mRNA and protein**
- **RP-A501 Preclinical Safety, Tox and Biodistribution Summary:**
  - No therapy-related deaths
  - No significant hematologic changes
  - No significant biochemical changes
  - No significant clinical chemistry changes
  - Mild and transient ALT elevation that self-resolved after one week in a single NHP
  - In both mouse and NHPs, VCN detection in Danon disease organs indicated high *LAMP2B* presence in heart tissue (for NHP, ~10x higher on average than in skeletal muscle and CNS)

RP-A501 Clinical Trial and Outcome Measures

Non-Randomized Dose-Escalation Phase 1 Study

Study Design

- Phase 1 open label study in male Danon patients
- Two age cohorts
  - Adolescent/Adult (>15 y)
  - Pediatric (8-14 y)
- Treatment doses
  - Low 6.7 x 10^{13} GC/kg
  - Higher 1.1 x 10^{14} GC/kg (removed going forward)

Primary Outcomes

- Assessment of:
  - Safety at all doses
  - Target tissue transduction & LAMP2B expression
  - Effect on cardiomyocyte histology
  - Clinical stabilization or improvement via cardiac imaging, serology and exercise testing

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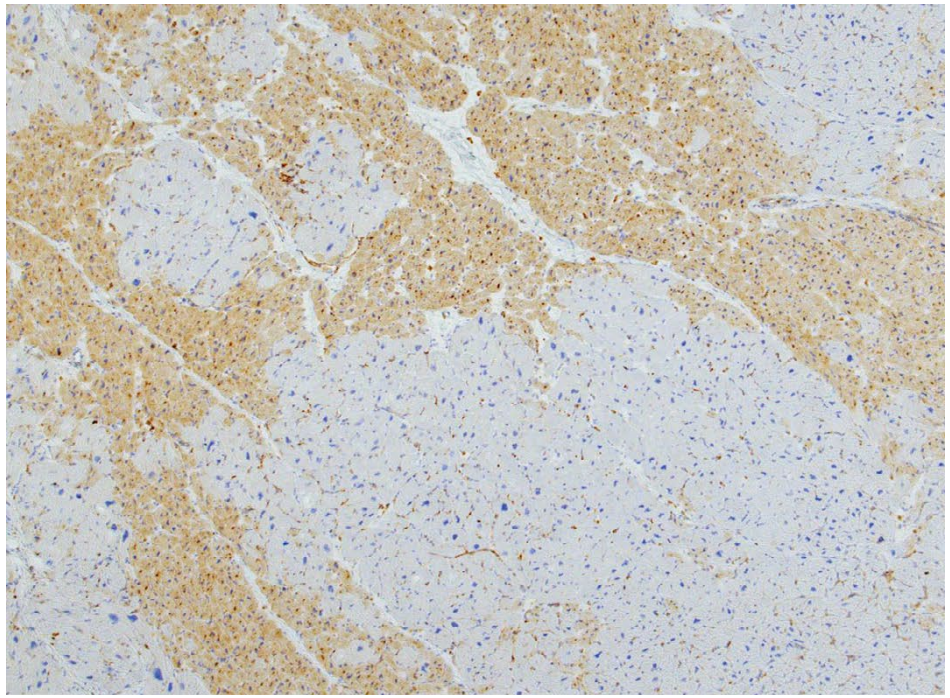
Natural History of Rapidly Progressing Heart Failure

Cardiac Clinical Features

- Progressive hypertrophic cardiomyopathy/heart failure
- Key Clinical Biomarker Changes
  - Echo:
    - Worsening diastolic parameters
      - ↑ left ventricular end diastolic diameter (LVEDD)
    - ↓ left ventricular fractional shortening (LVFS)
    - ↑ ventricular wall thickness
    - ↓ left ventricular ejection fraction (LVEF) is late event
  - Hemodynamics: Decreasing cardiac output and/or stroke volume
  - Biomarkers: Elevated BNP, CK-MB, troponin

Female Danon Cardiac Histology Suggests Broad LAMP2 Expression Important for Reversal of Phenotype

- Immunohistochemistry (IHC) from Danon female patients with severe disease display large patches negative for LAMP2 expression
- Broad expression of LAMP2 is likely the key to correcting phenotype rather than overall protein levels
- Based on this data, IHC demonstrating broad and ***homogeneous cardiac expression may be the best predictor of long-term efficacy***



Cardiac IHC Staining in Female Danon Patient Requiring Transplant at 10 y[1]

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1. *Oldfors et al 2015*

RP-A501: Patient Entry Criteria

Inclusion

- Male
- Confirmed *LAMP2B* mutation
- Cardiac involvement confirmed by echocardiogram, MRI or ECG
- NYHA Class II or III symptoms
- Ability to walk >150 meters unassisted during the 6-minute walk test (6MWT)
- **Adequate hematologic, hepatic and renal function***
- Capacity to provide informed consent
- No contraindication for meningococcal vaccination (prior to RP-A501 administration)

Exclusion

- Anti-AAV9 neutralizing antibody titer criteria
- **LVEF <40% at baseline**
- Acute or chronic respiratory failure on ventilatory support
- IV inotropes, vasodilators or diuretics within 30 days prior to enrollment
- Prior or current LVAD
- Prior organ transplantation
- Prior cardiac surgery or percutaneous cardiac intervention (for arteriothrombotic complications or valvuloplasty)
- **History of stroke or TIA**

*Additional details @ClinicalTrials.gov, Bold indicates protocol updates

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RP-A501: Baseline Clinical Status and Biomarker Values

Cohort	Patient ID	Age at Enrollment	Weight (kg)	Clinical Status		Biomarker
				NYHA Class	Six Minute Walk (meters)	BNP [<100 pg/mL]
Adult - Low Dose	1001	17 years	52.2	II	443	70
	1002	20 years	89.1	II	405	1104
	1005	18 years	91.8	II	427	161
Adult - High Dose	1006	21 years	82.7	II	436	123
	1007	20 years	96.7	II	434	630

RP-A501: Baseline Patient Status

Hypertrophic Cardiomyopathy

1. Thickened myocardium
   - LV posterior wall
   - Interventricular septum
2. Preserved systolic function until late stage of disease
   - LV Ejection fraction
   - Cardiac output
3. Impaired diastolic function
   - Pulmonary capillary wedge pressure

Cohort	Patient ID	Age at Enrollment	Weight (kg)	Echocardiogram		Catheterization
				Wall Thickness* [6-11 mm]	LV EF** [50-75%]	PCWp [8-12 mmHg]
Adult - Low Dose	1001	17 years	52.2	16.4	62	11
	1002	20 years	89.1	22.4	59	19
	1005	18 years	91.8	17	59	13
Adult - High Dose	1006	21 years	82.7	15	47	14
	1007	20 years	96.7	22.7	35	26

* Wall thickness refers to left ventricular posterior wall in diastole (LVPWd)

** All echocardiographic parameters from local site assessment: LVEF=left ventricular ejection fraction

PCWp = pulmonary capillary wedge pressure

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RP-A501: High Dose Summary of Safety and Tolerability

High Dose Adult and Adolescent
Age ≥15 years
$1.1x10^{14}$ GC*/kg

n=2*

Immediate:	n
Fever	1
Fatigue	2
Constipation	1
Nausea/vomiting	1

Early:	n
Complement activation	1**
Thrombocytopenia	2★
Transaminase elevation	2
D-dimer elevation	1
TMA w/ acute kidney injury	1**

Delayed:	n
Transaminase elevation	1
Deep vein thrombosis	1
Steroid-induced myopathy	1
Ventricular arrhythmias	1
Acute heart failure	1

Currently-Implemented Protocol Risk Mitigation:
- No further enrollment at HIGHER dose
- Adjusted immunosuppressive regimen
  - Corticosteroids: Limit daily dose
  - Sirolimus: Minimize renal impact
  - Frequent monitoring for early signs of TMA
  - Rituximab continued

* No further enrollment at this dose
** Patient developed thrombotic microangiopathy (TMA) with acute renal failure requiring transient hemodialysis with complete renal function recovery
★ All Grade 1, except for Grade 4 in patient who developed TMA Red colored font indicates Serious Adverse Event (SAE)

RP-A501: Low Dose Summary of Safety and Tolerability

Low Dose Adult and Adolescent
Age ≥15 years
$6.7x10^{13}$ GC*/kg

n=3

Immediate:	n	Early:	n	Delayed:	n
Fever	1	Complement activation	2*	Transaminase elevation	2
Fatigue	1	Thrombocytopenia	2★	Steroid-induced myopathy	2
Constipation	2	Transaminase elevation	3	Salmonella Sepsis	1
Nausea/vomiting	3	D-dimer elevation	3		

RP-A501 was well tolerated and all adverse events in low & high dose adult/adolescent cohorts were reversible demonstrating a manageable safety profile

* Not monitored for in initial patient

★All Grade 1

Red colored font indicates Serious Adverse Event (SAE)

RP-A501: Stabilization or Improvement of Cardiac Biomarkers and Functional Status Across Dose Levels

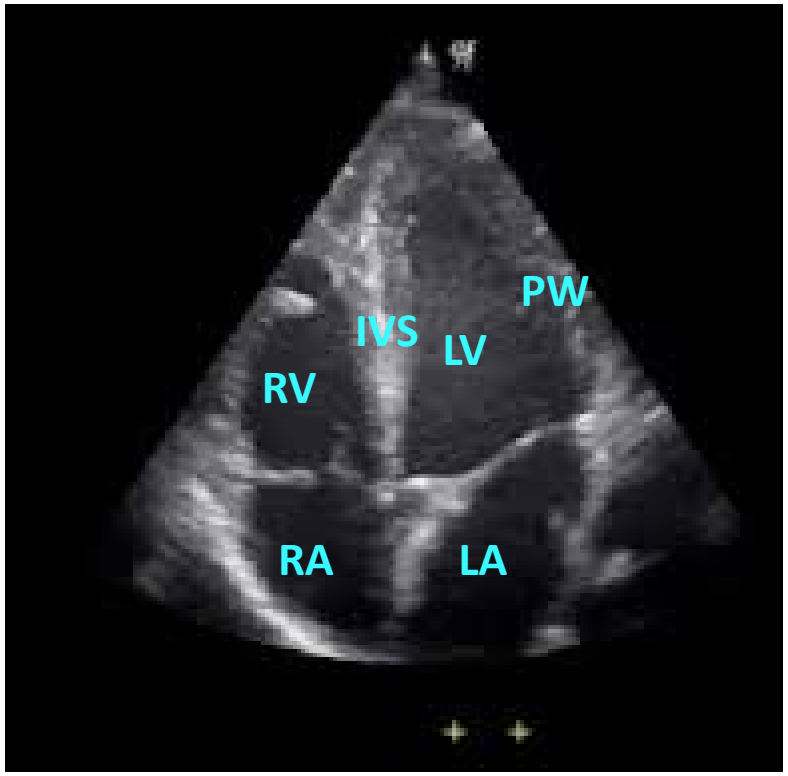
Cohort	Patient ID	Variable	Baseline	Most Recent Follow-up	Time of Follow-up
Adult - Low Dose	1001*	NYHA class	II	II	24 months
		BNP (pg/mL)	70	30	
		6 MWT (meters)	443	467	
	1002	NYHA class	II	I	18 months
		BNP (pg/mL)	942	200	
		6 MWT (meters)	405	410	
	1005	NYHA class	II	I	15 months
		BNP (pg/mL)	176	44	
		6 MWT (meters)	427	435	
Adult - High Dose	1006	NYHA class	II	I	12 months
		BNP (pg/mL)	123	41	
		6 MWT (meters)	436	492	

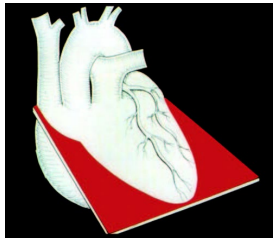
* Corticosteroid compliance not monitored in initial patient
NYHA = New York Heart Association

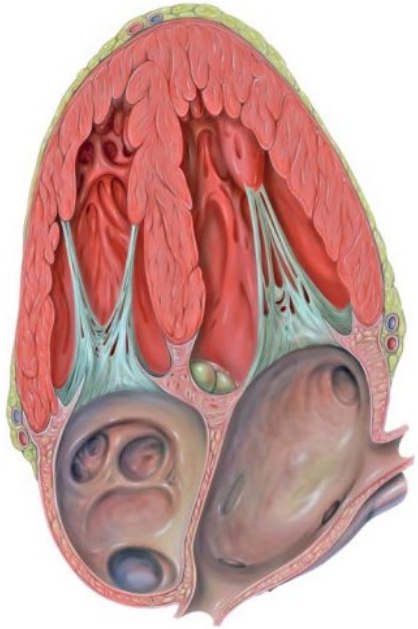
BNP = Brain Natriuretic Peptide
6MWT = 6-Minute Walk Test

RP-A501 Adolescent and Adult: Echocardiogram (Apical 4-Chamber View)

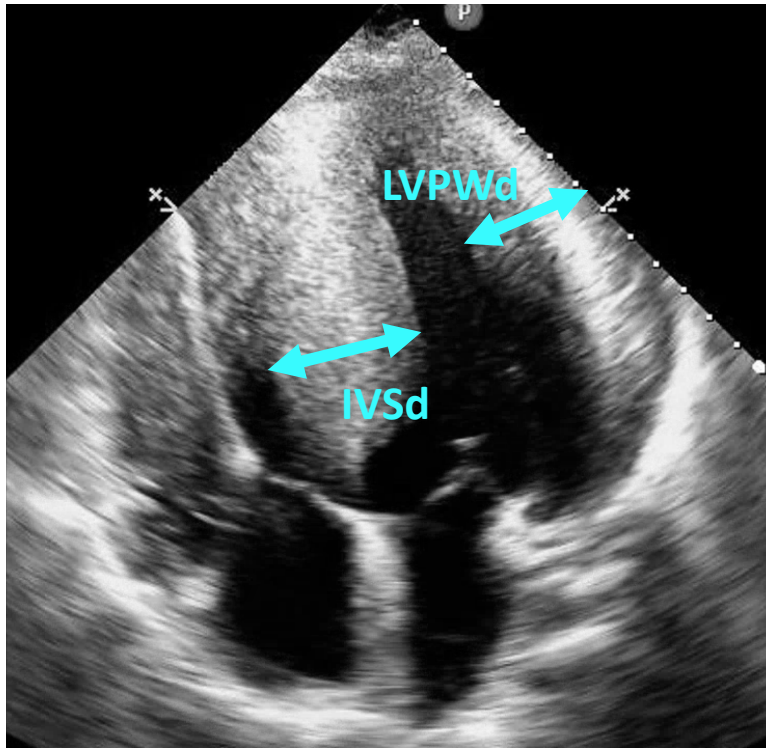
Normal







Danon Patient 1002

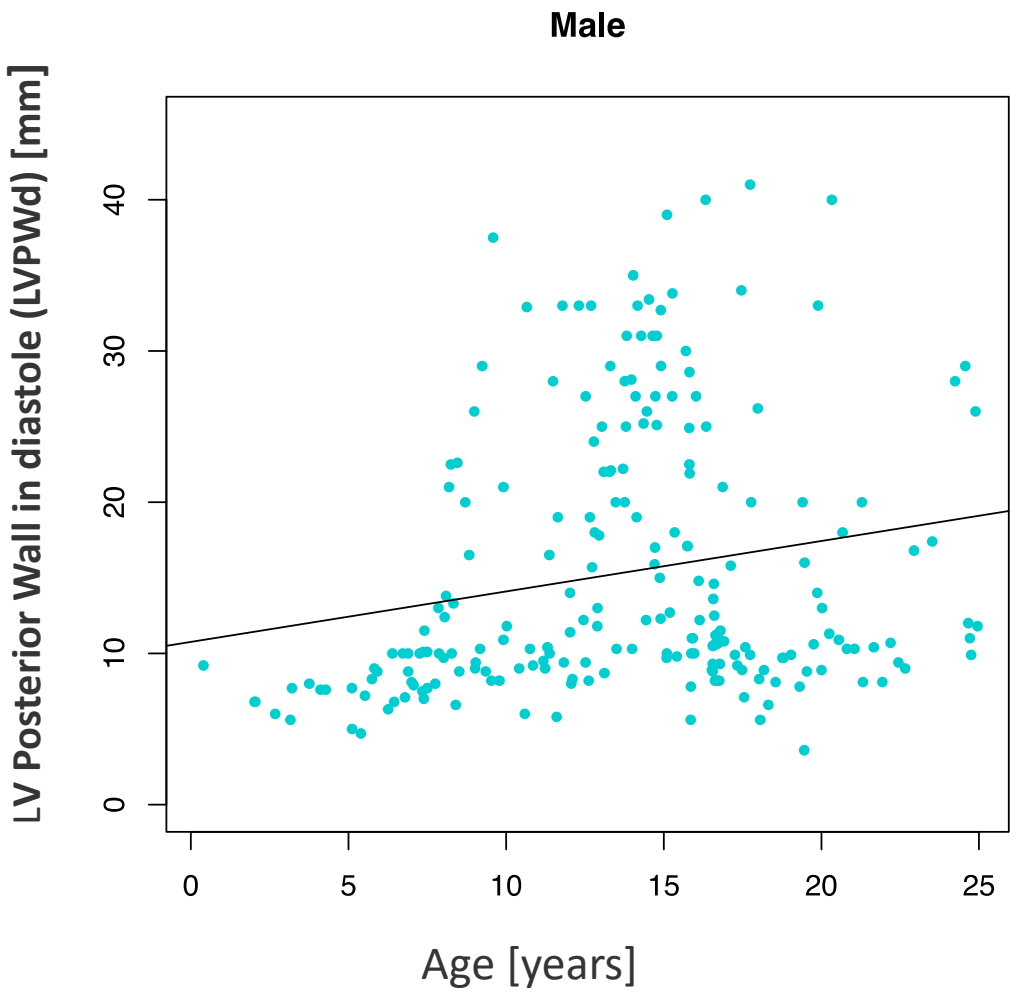


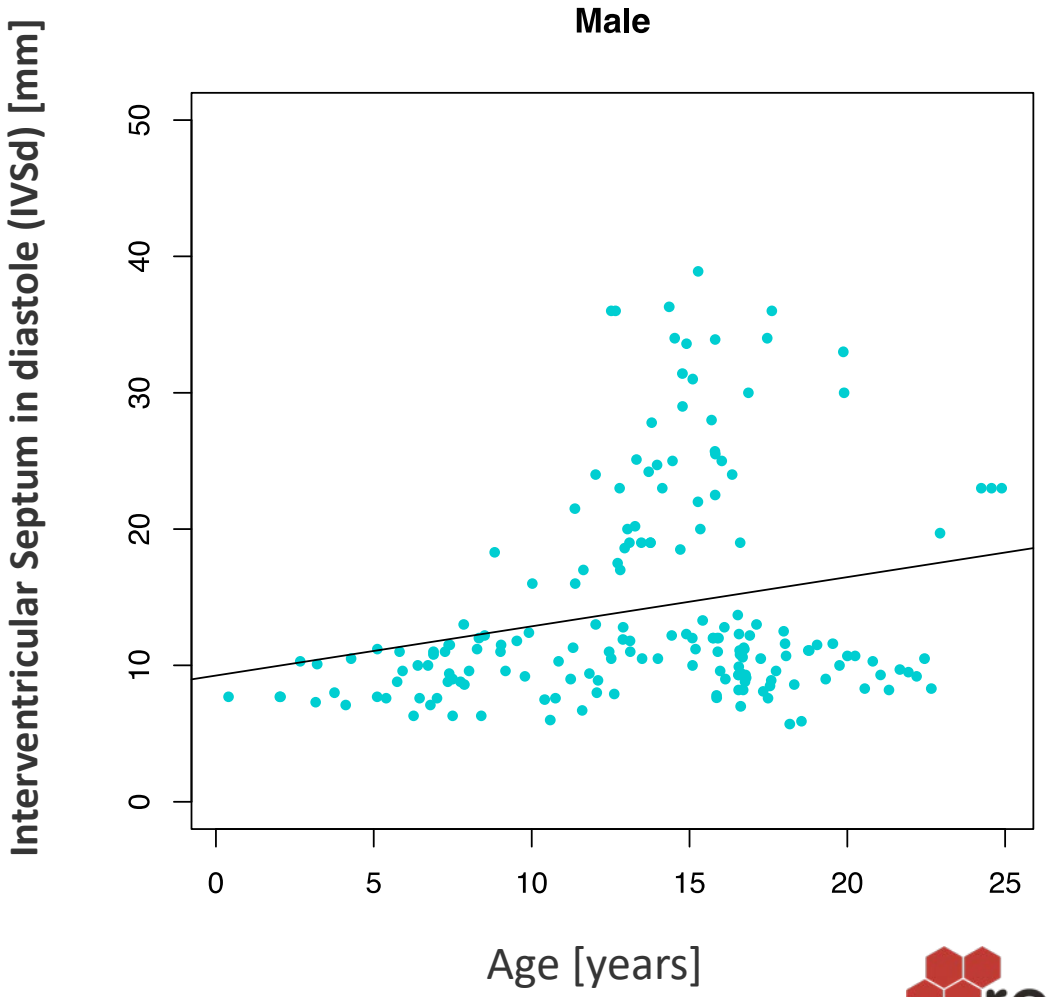
RA: right atrium
RV: right ventricle
IVS: interventricular septum

LA: left atrium
LV: left ventricle
PW: posterior wall

LVPWd: LVPW in diastole
IVSd: IVS in diastole

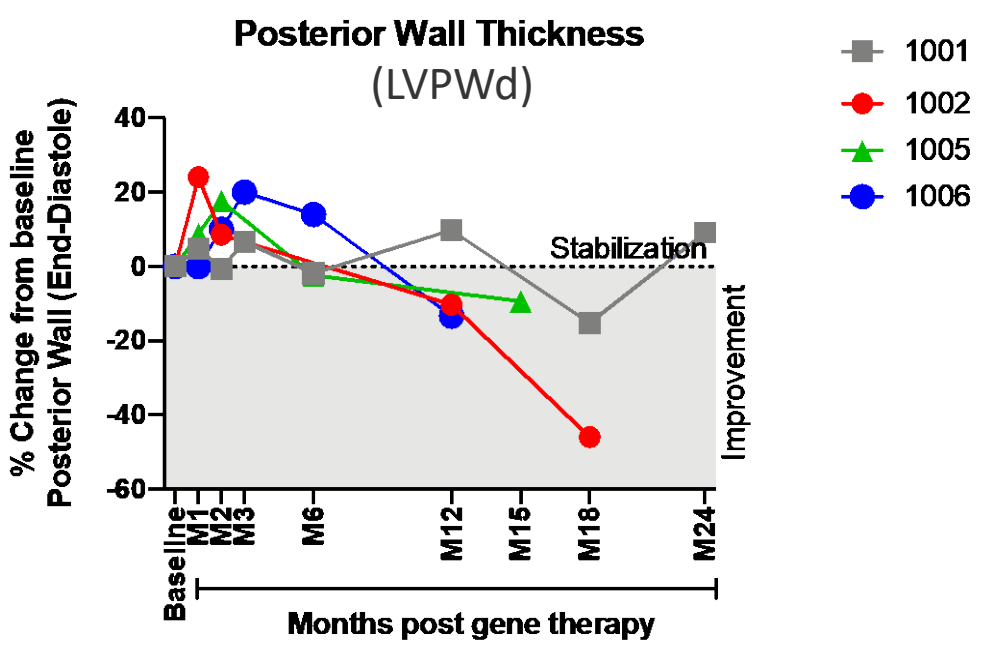
Danon Natural History: LV Posterior & Septal Wall Thickness (Echo)

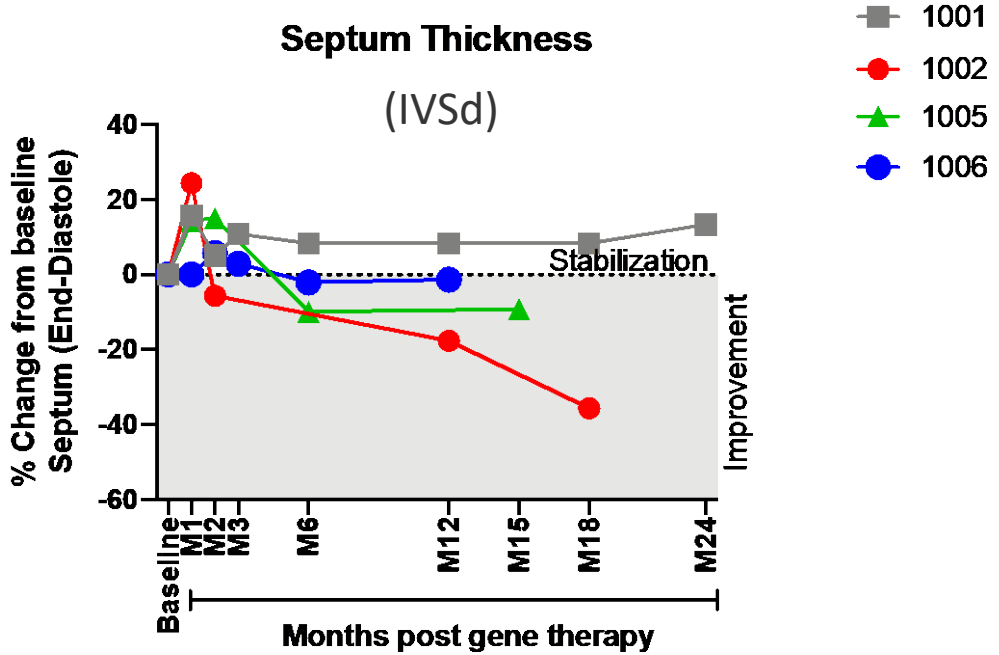


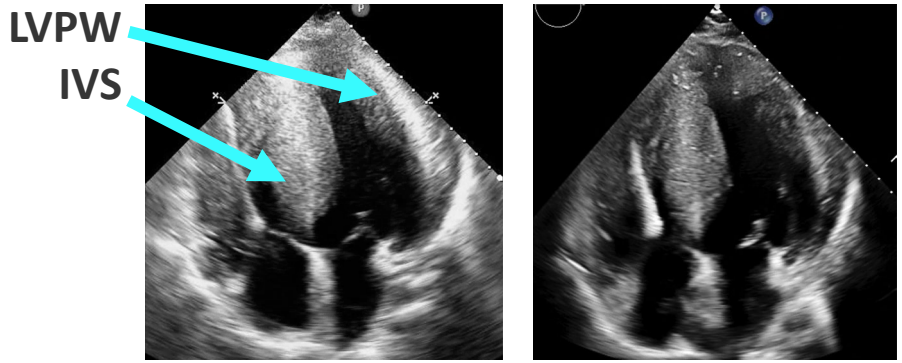


Retrospective Review of Echocardiograph Data from N=32 Male Danon Patients

Remodeling of Ventricular Hypertrophy on Echocardiography

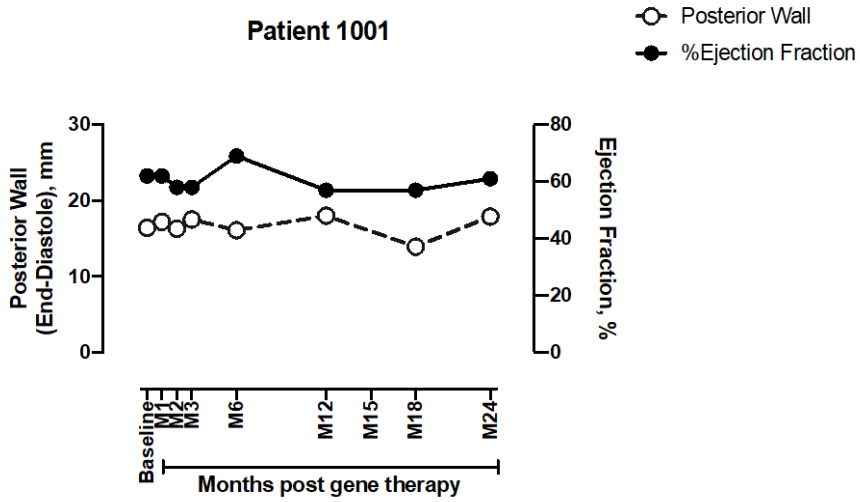


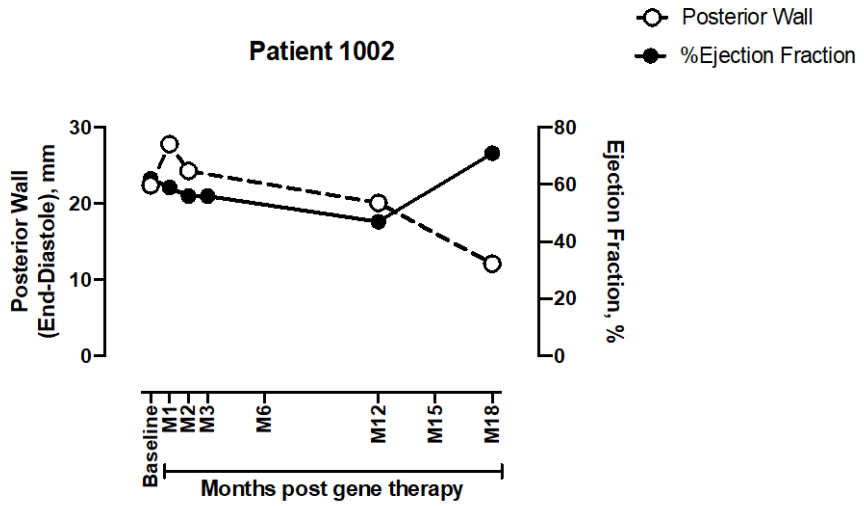


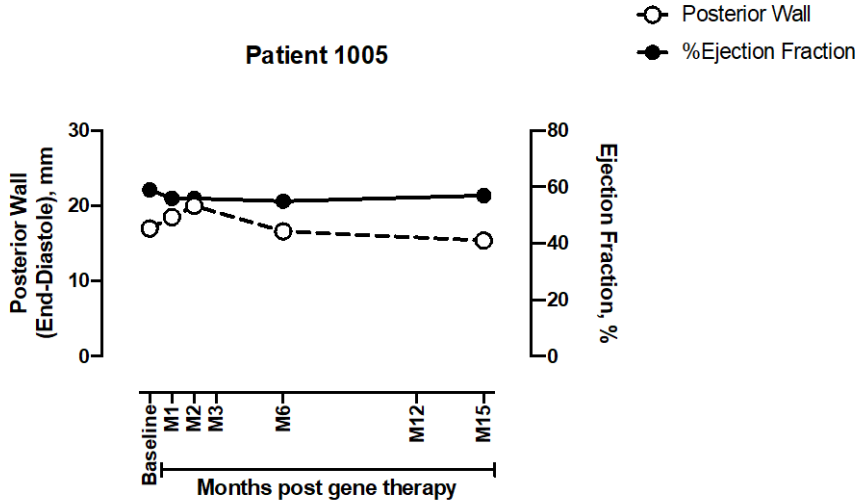


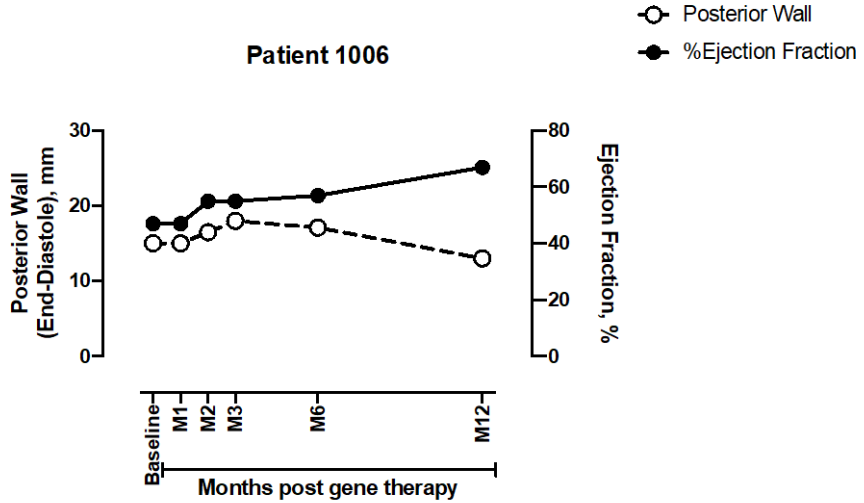
All echocardiographic parameters from local laboratory assessment, conducted by a single reader

Stabilization or Improvement of LV EF and Wall Thickness



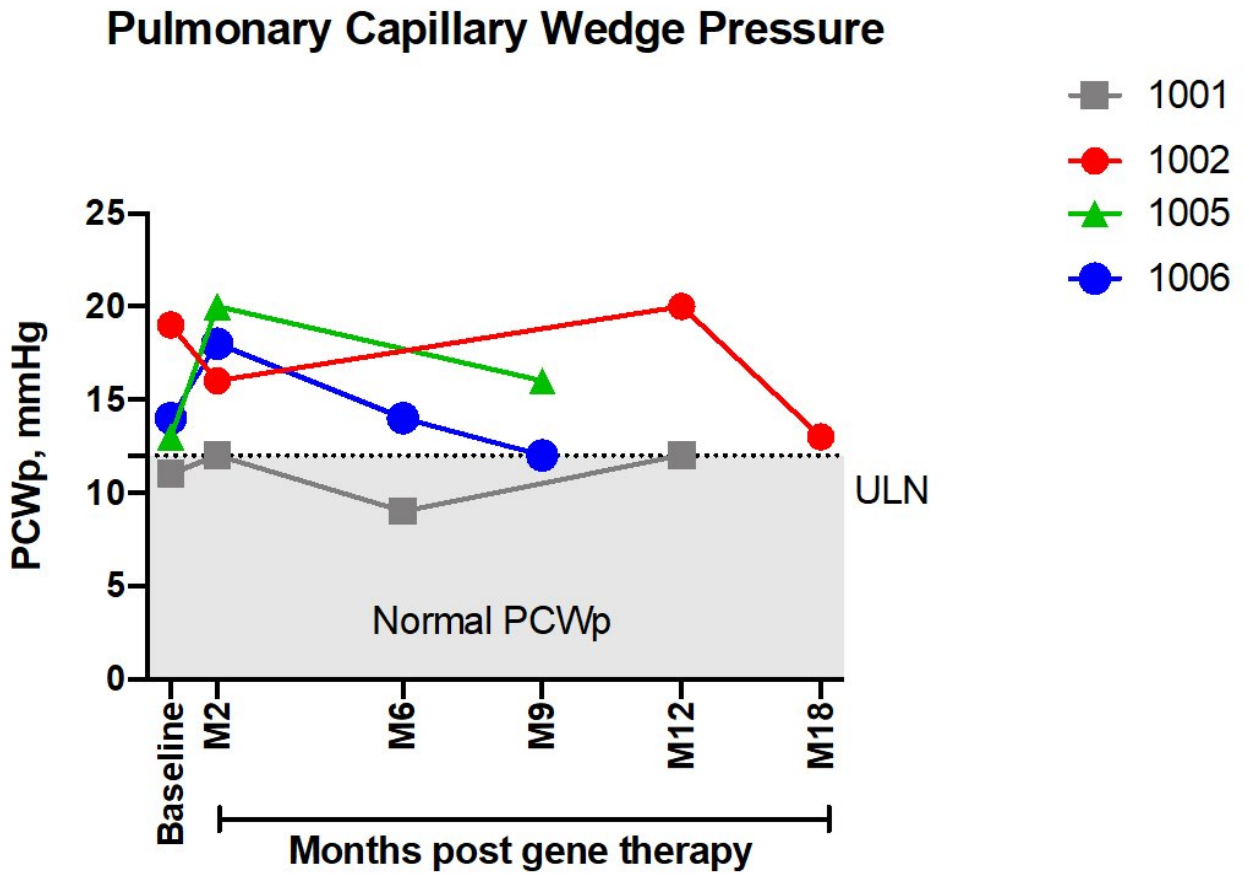




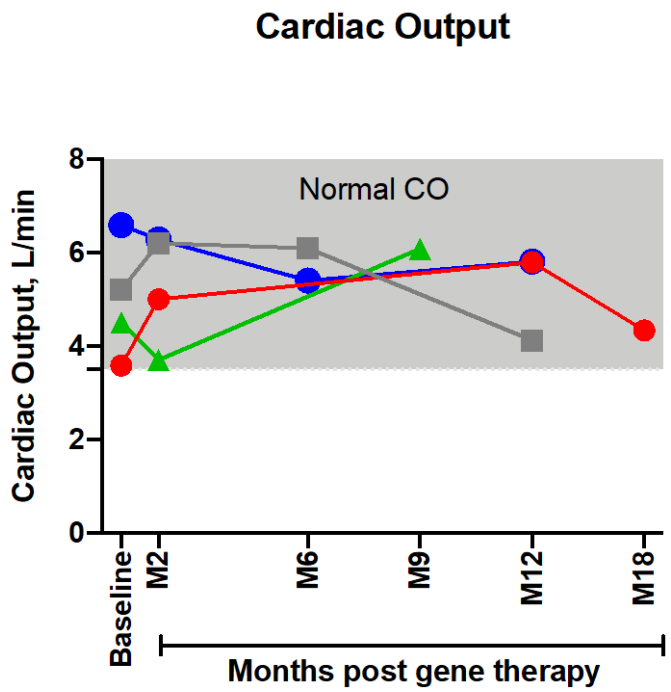


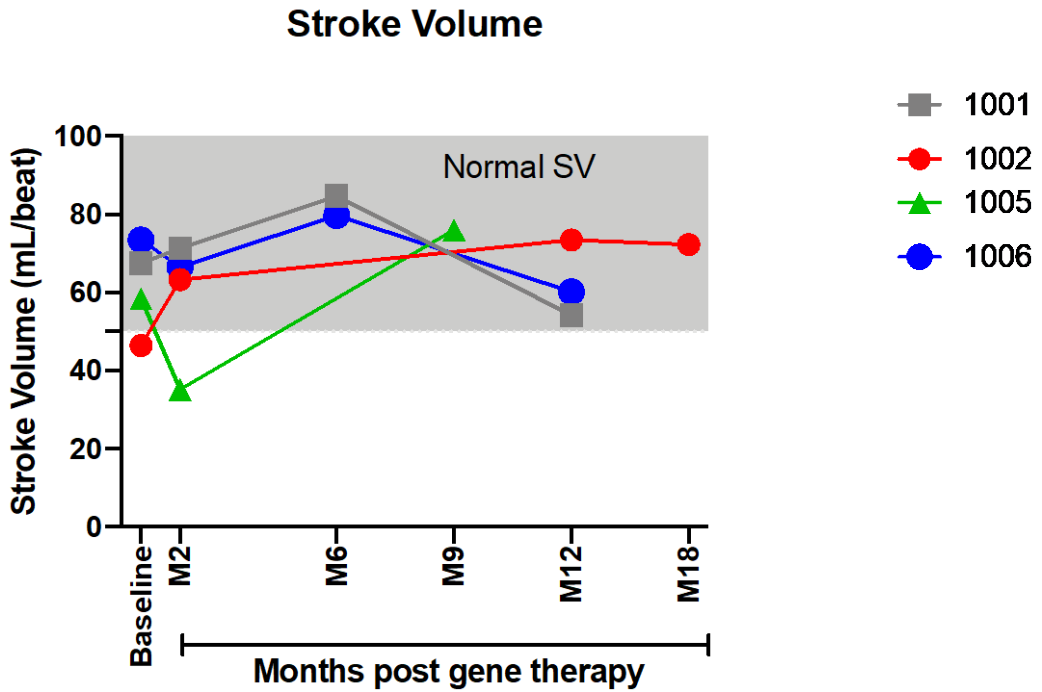
All echocardiographic parameters from local laboratory assessment, conducted by a single reader

Invasive Hemodynamics Demonstrated Long Term Stabilization or Improvement of Diastolic Dysfunction (LV Filling Pressure)



Hemodynamic Stabilization of Systolic Function





Cardiac Output = Stroke Volume x Heart Rate

RP-A501 Demonstrated Stable Cardiac Vector Copy Numbers (VCN)

Cohort	Patient ID	Cardiac VCN	
		Week 8	Month 12
Adult - Low Dose	1001*	0.5	0.6
	1002	6.5	1.5
	1005	2.5	1.9[1]
Adult - High Dose	1006	3.9	1.1
	1007	5.9	6.8 (RV)[2] 9.2 (LV)[2]

[1] Month 9 data
[2] Explanted heart samples at Month 5

* Patient 1001 was only locally monitored for compliance for two weeks; longer compliance monitoring initiated after 1001
VCN=Vector Copies per diploid nucleus

Endomyocardial LAMP2B Protein Expression by **Immunohistochemistry (IHC)**

Cohort	Patient ID	LAMP2B Protein Expression (by IHC)**	
		Week 8	Month 12
Adult - Low Dose	1001*	7.3%	2.5% (Previously <15%)[1]
	1002	36.9%	67.8%
	1005	17.6%	92.4%[2]
Adult - High Dose	1006	5.0%	100%
	1007	6.9%	100%[3]

[1] Previously disclosed as a range due to high variance, now clarified
[2] Month 9 data
[3] Explant sample at Month 5

* Patient 1001 was only locally monitored for compliance for two weeks; longer compliance monitoring initiated after 1001
** Endomyocardial biopsies stained for LAMP2 compared to normal control samples. Percent area of cell staining was quantitated using software in a blinded fashion from 2 to 14 sections. Qualitative assessment reported for samples with high variance.

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Endomyocardial LAMP2B Western Blot Protein Expression

Cohort	Patient ID	LAMP2B Protein Expression (by Western Blot)	
		Week 8	Month 5-18
Adult - Low Dose	1001	20.7%	17.9%[1]
	1002	27.3%	21.2%[2]
	1005	42.8%	61.1%[3]
Adult – High Dose	1006	14.6%	18.2%[1]
	1007	25.0%	RV: 45.1%[4] LV: 44.0%[4]

[1] Month 6 data; inadequate sample at Month 12
[2] Month 18 data; inadequate sample at Month 12
[3] Month 9 data
[4] Explanted heart; Month 5 data

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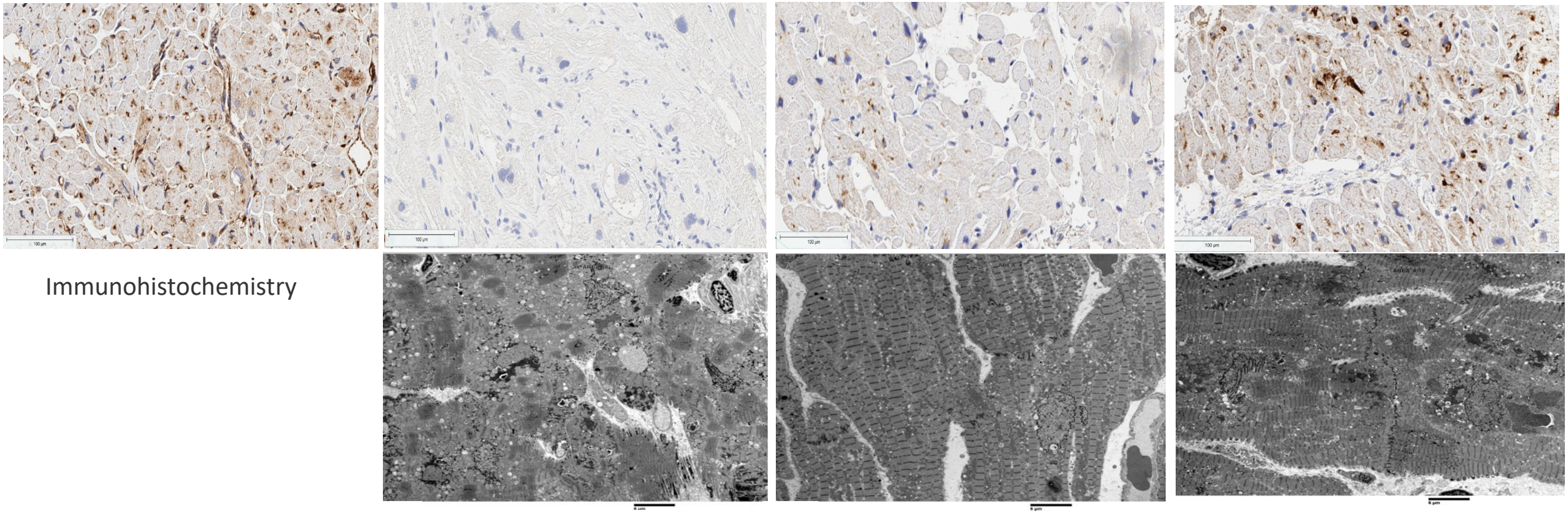
RP-A501 Low Dose: LAMP2 Protein Expression by Immunohistochemistry and Cell Morphology by Electron Microscopy

Normal Control

Baseline

Week 8

Month 9



Immunohistochemistry

Electron Microscopy

Representative images from patient 1005 from biopsy of IVS

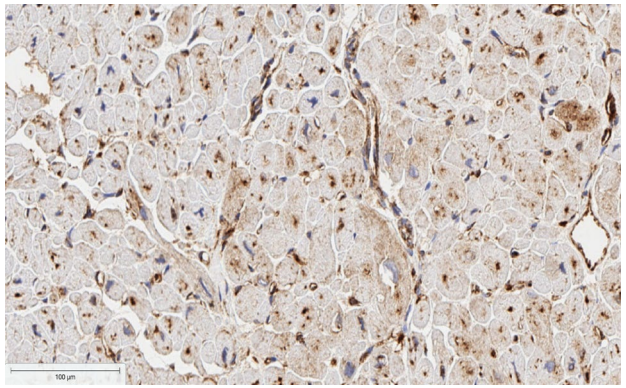
RP-A501 High Dose: LAMP2 Protein Expression by Immunohistochemistry and Cell Morphology by Electron Microscopy

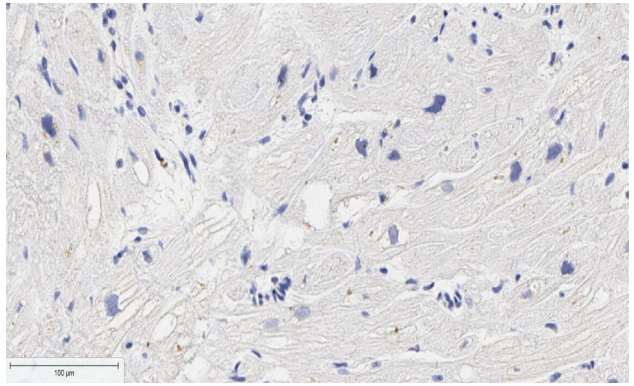
Normal Control

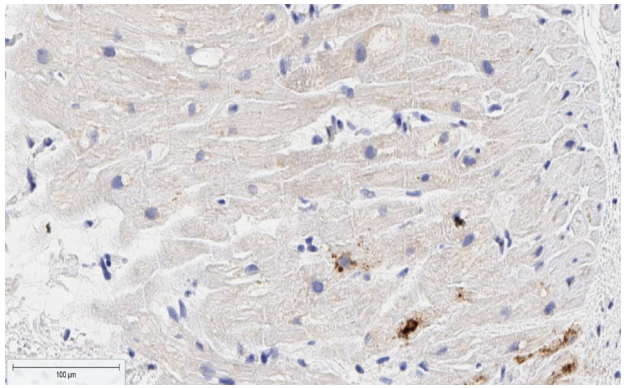
Baseline

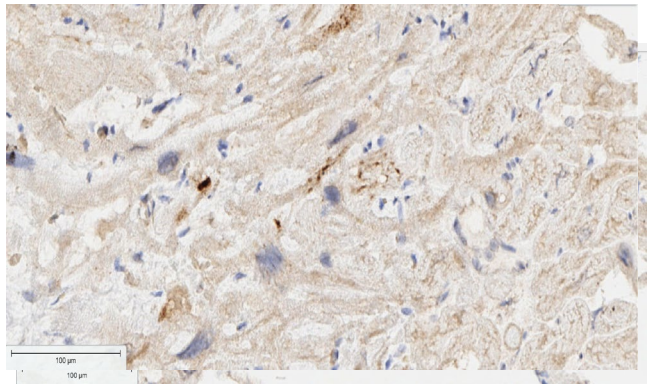
Week 8

Month 12

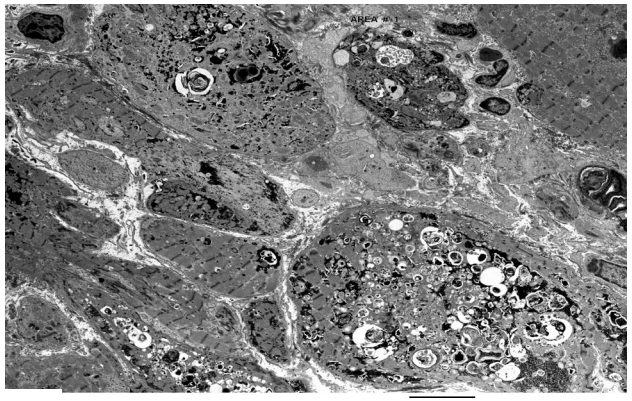


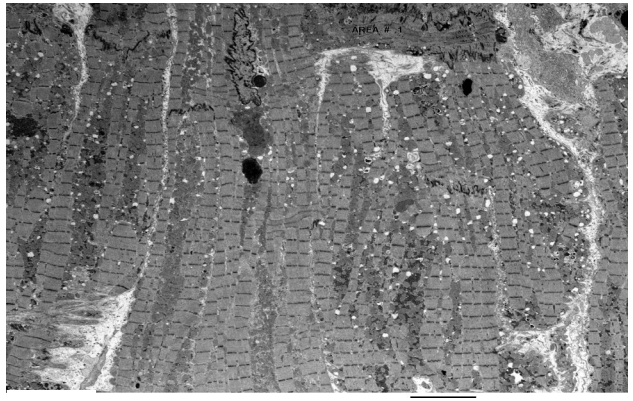


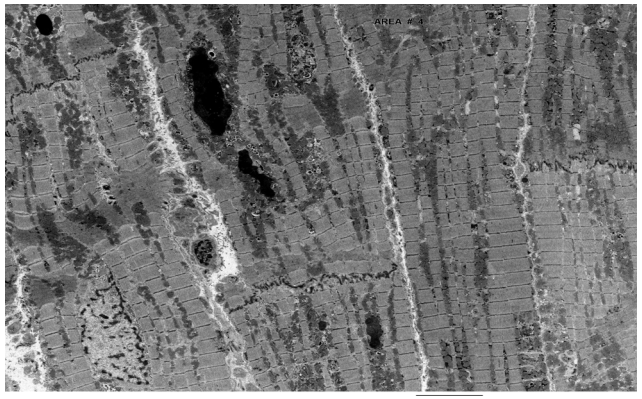




Immunohistochemistry



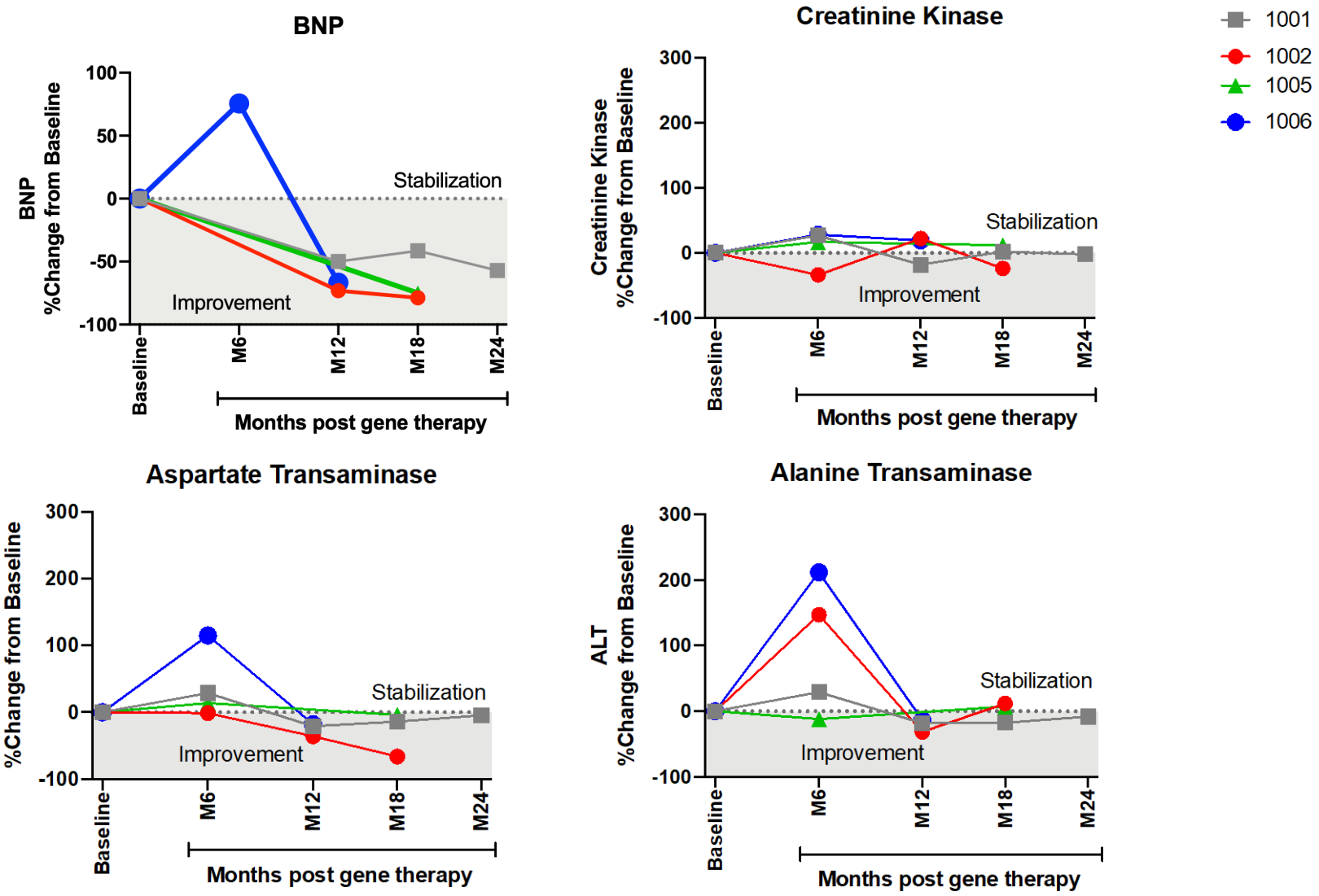




Electron Microscopy

Representative images from patient 1006 from biopsy of IVS

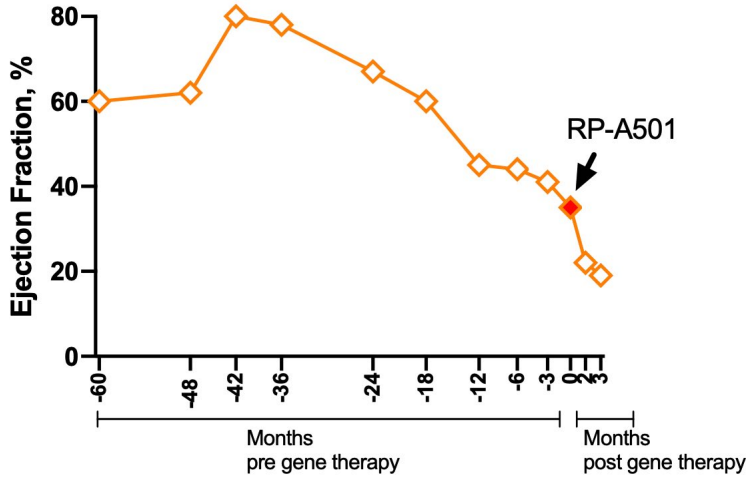
RP-A501: Stable or Improved Clinical Biomarkers

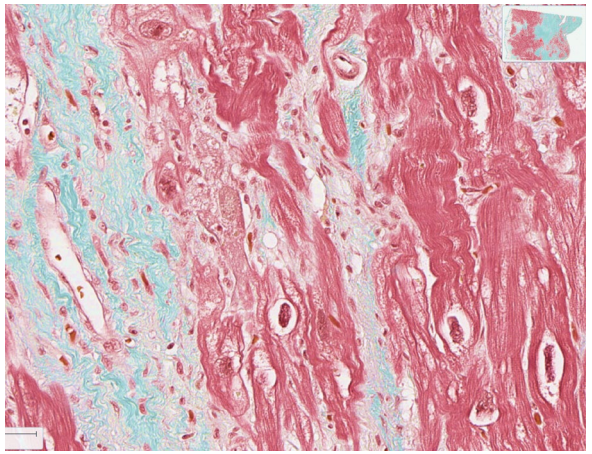


RP-A501 High Dose: Patient 1007 Danon Disease Progression

20 Year-old Male Danon Patient

- **Baseline risk factors suggest "point of no return" in Danon disease progression**
  - Diminished LV EF (35%)
  - Markedly elevated LV filling pressure (PCWp 26 mmHg)
  - Prior evidence of fibrosis on MRI
- **Continued cardiac Danon disease progression**
  - LV EF continued to decrease
  - Increased frequency of ventricular arrhythmias
- Uncontrolled arrhythmias resulting in decompensated heart failure; patient received heart transplant (Month 5)
  - **Danon Disease progression determined as primary cause**



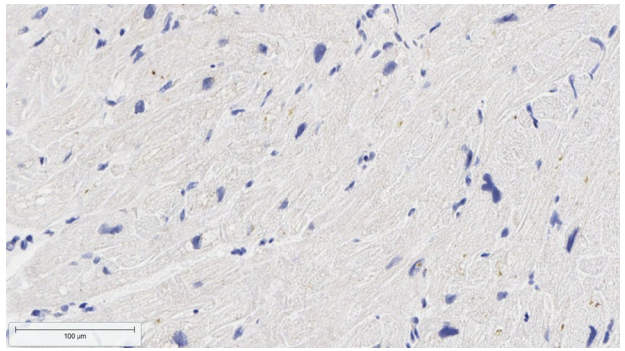


Trichrome Stain of Explanted LV

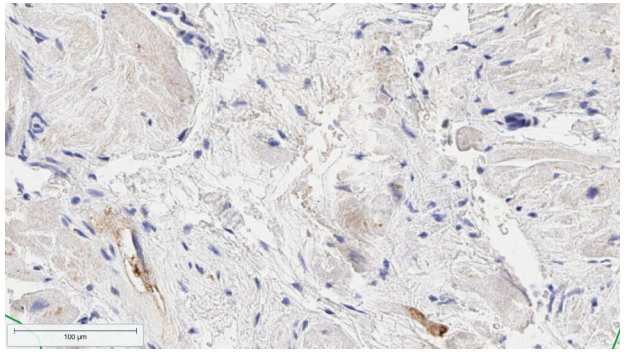
- Severe fibrosis
- No evidence of inflammation

Patient 1007 Predose and Explanted Heart Myocardial Tissue*

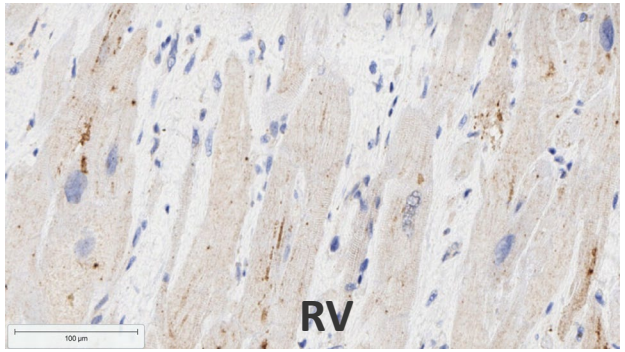
Pre-Dose Biopsy (IVS)

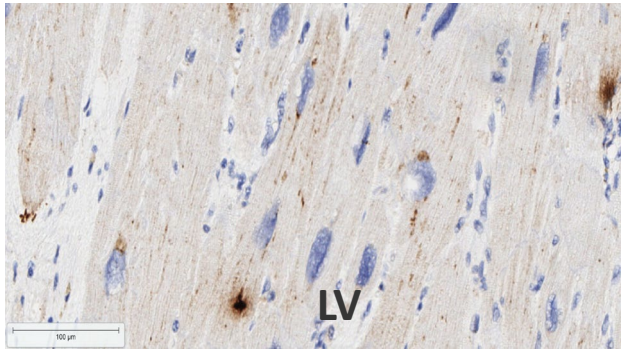


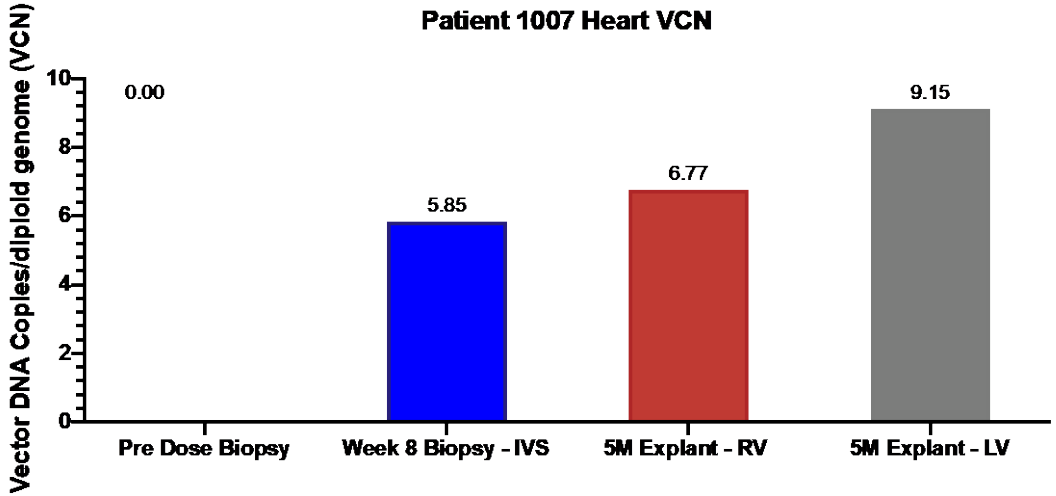
Week 8 Biopsy (IVS)



Explanted Heart – 5M post treatment







Patient ID	LAMP2B Protein Expression (by IHC)		
	Week 8	Month 5 Explant RV	Month 5 Explant LV
1007	6.8%	100%	100%

* Atrial VCN and LAMP2 expression was consistent with ventricular expression (100%)
IHC = Immunohistochemistry

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RP-A501 High Dose Adult and Adolescent Cohort Summary (N=2)

- **RP-A501 r-AAV dose-dependent toxicity was seen at 1.1x10^{14} GC/kg dose levels**
  - One of two patients developed thrombotic microangiopathy (TMA)
    - Acute renal failure managed with hemodialysis and eculizumab
    - Baseline LV systolic failure may have contributed
    - Largest patient in clinical trial (>90kg) who received highest total dose (1.06 x 10^{16} GC)
- **Histologic evidence of LAMP2B gene expression that is sustained**
  - Cellular level (explanted heart)
    - Robust expression in key target areas of heart (ventricles)
    - Improved LAMP2B protein expression
    - Higher expression relative to endomyocardial biopsies (EMB)

Clinical parameters improved or remained stable (comparable to low dose cohort) in high dose patient treated before end-stage Danon disease (1007)

Note: Higher doses (1.1e14 and higher) removed moving forward; will focus on *lower dose given positive benefit/risk*

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RP-A501 Low Dose Adult and Adolescent Cohort Summary (N=3)

RP-A501 r-AAV generally well tolerated at $6.7x10^{13}$ GC/kg dose level

- Tailored immunosuppressive regimen
- Reversible immunologic response with no lasting clinical sequelae

Clinical parameters improved or remained stable

- Functional and Biomarker Parameters
  - NYHA class improved or stabilized
  - 6-minute walk distance mildly improved or stabilized
  - BNP decreased or stabilized
- Echocardiograph Parameters
  - LV wall thickness decreased or stabilized
  - Improved or stable ejection fraction by 12 months
- Hemodynamic Parameters
  - Cardiac output remained normal with stable or improved left heart filling pressures (Pulmonary wedge)

Histologic evidence of LAMP2B gene expression that is sustained

- Stable and robust LAMP2B protein expression
- Decreased vacuoles and improved architecture on electron microscopy

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Leukocyte Adhesion Deficiency-I (LAD-I)
Monogenic Immunodeficiency Disorder

RP-L102
Fanconi Anemia

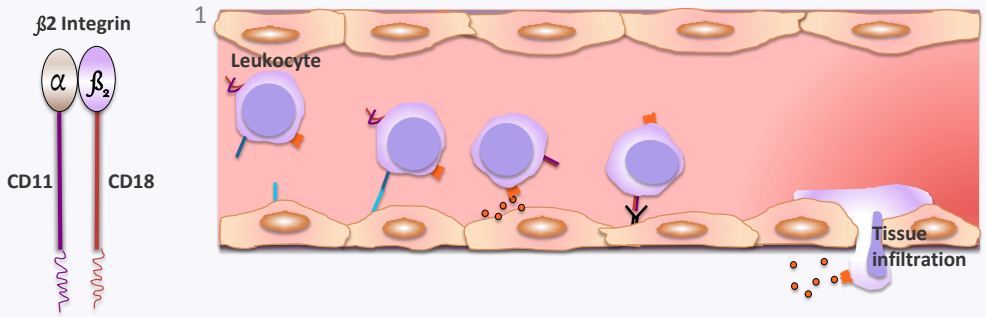
RP-A501
Danon Disease

RP-L201
Leukocyte Adhesion Deficiency-I

RP-L301
Pyruvate Kinase Deficiency

RP-L401
Infantile Malignant Osteopetrosis

OVERVIEW:



Background: Disorder characterized by recurring and ultimately fatal infections caused by *ITGB2* gene mutations

- ***>50%*** patients with severe variant: ***60-75% mortality by age 2***

Current Available Treatments: Allogeneic hematopoietic stem cell transplant associated with significant graft failure and acute GVHD

Addressable Market: Estimated ***25-50 pts*** treatable per year for severe population; up to 100 for potential expansion into moderate population in the US + Europe with effective gene therapy

RP-L201: Preclinical studies show stable engraftment and phenotypic correction in murine models, with restored neutrophil migration capability

Regulatory Designations: Fast Track and Rare Pediatric Disease designations in the U.S.; Advanced Therapy Medicinal Product (ATMP) classification in EU; Orphan Drug designation in the U.S./EU

[1] Defective expression of ß2 integrin on leukocytes limits their extravasation to inflamed sites.

LAD-I Program Summary

Ultra-rare Disease = Streamlined Regulatory Approach

Potential design & clinical endpoints:

- **Target Patient Population:** Severe LAD-I patients (CD18<2%), ~2/3 mortality by 2y
- **Control:** Literature review of ~300 pts. (Rocket/academic collaborative publication[1])
- **Potential Clinical Endpoints**: Modest correction of CD18 expression, survival

Efficacy Trials & Registration Status – Ahead of Schedule

Registration & study planning on-schedule:

- ✓ Orphan Drug (US/EU) and Pediatric Rare Disease (US) designations granted
- ✓ IND & Phase 1/2 cleared by FDA
- ✓ Spain IMPD cleared
- ✓ US PI (UCLA Dr. Don Kohn)
- ✓ Recruitment underway from around the globe
- ✓ 3 global sites planned in the US/EU

Product/Manufacturing Optimization

Process now optimized:

- ✓ VCN using GMP vector with transduction enhancers consistently ~3 (Target VCN >1)

[1]Almarza Novoa E, Kasbekar S, Thrasher AJ, Kohn DB, Sevilla J, Nguyen T, Schwartz JD, Bueren JA. Leukocyte adhesion deficiency-I: A comprehensive review of all published cases. J Allergy Clin Immunol Pract. 2018 Jan 20. pii: S2213-2198(17)31026-7. doi: 10.1016/j.jaip.2017.12.008.

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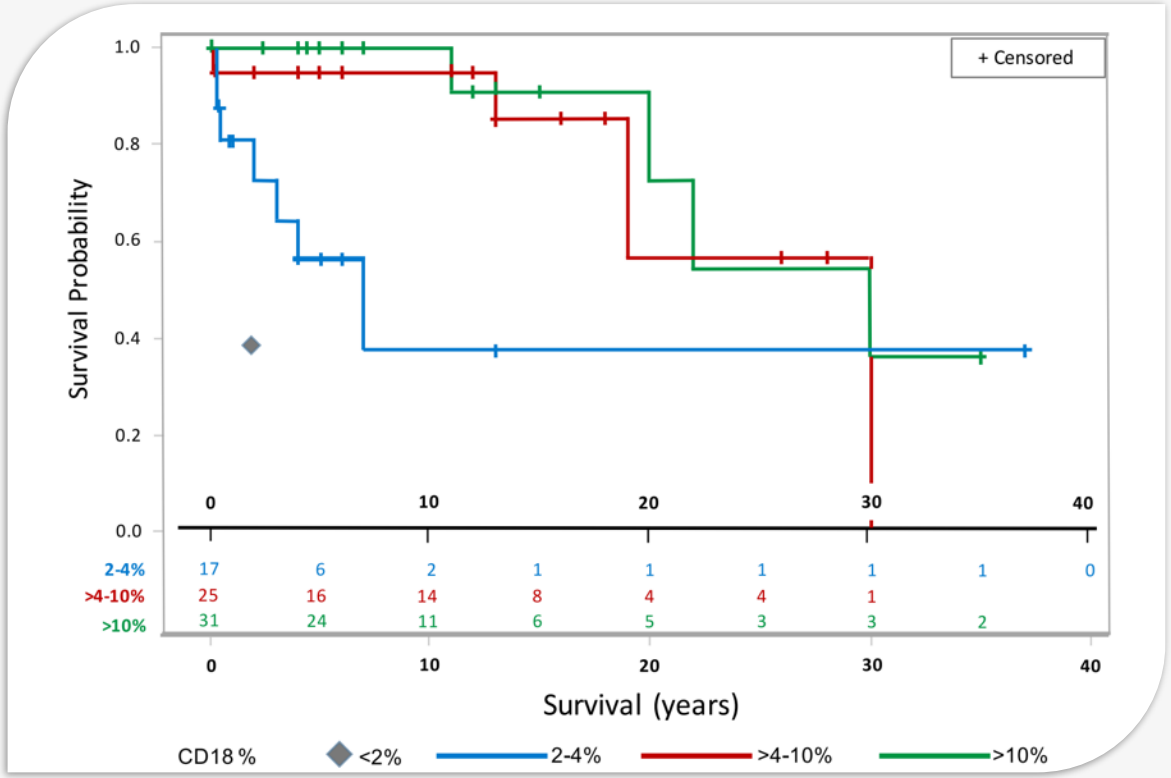
Rationale for Gene Therapy in LAD-I: CD18 Expression Correlates to Patient Survival

Kaplan-Meier Survival Estimates by Neutrophil CD18 Expression

-Patients with moderate LAD-I not receiving allogeneic HSCT-



Natural history studies show the ***correlation*** between ***higher CD18*** expression and longer patient ***survival,*** supporting gene therapy's potential in LAD-I patients

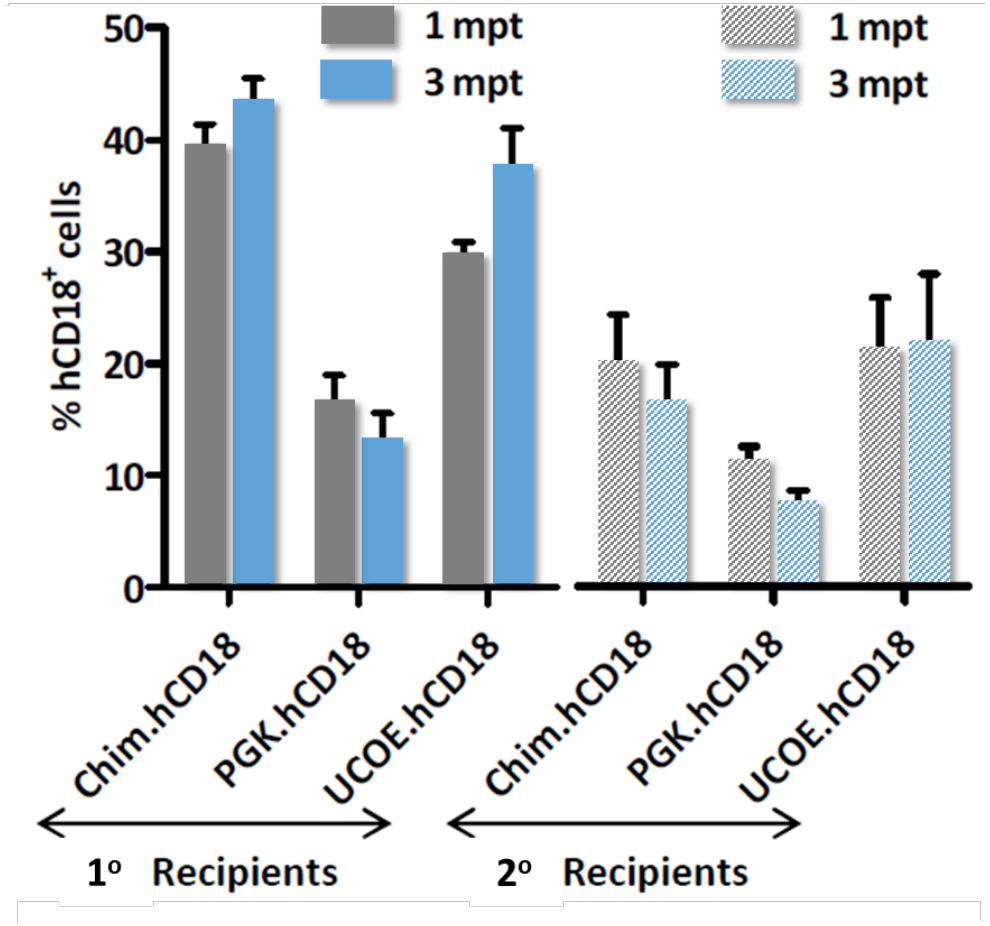
The grey diamond indicates the 39% survival to age 2 years for 66 evaluable patients with severe LAD-I not receiving HSCT

Poster Presentation at ASGCT May 2018

Source: Almarza Novoa E et al. J Allergy Clin Immunol Pract. 2018 Jan 20. pii: S2213-2198(17)31026-7. [Epub ahead of print]

LAD-I: Mouse Study Shows LAD-I Correction

- Primary and serially transplanted LAD mice underwent CD18 lenti GTx with different promoters
- Myeloablative conditioning was used
- Rocket chose the Chimeric cFES/CTSG (myeloid-specific) promoter (Post-transplant PB VCN 0.4-0.9)



Leon-Rico D, Aldea M, Sanchez-Baltasar R, Mesa-Nuñez C, Record J, Burns SO, Santilli G, Thrasher AJ, Bueren JA, Almarza E. Hum Gene Ther. 2016 Sep;27(9):668-78. doi: 10.1089/hum.2016.016. Epub 2016 May 5.

RP-L201 (LAD-I) Clinical Trial and Outcome Measures[1]

Non-Randomized Phase 1/2 Study

Design

- Enroll 9 pediatric patients globally
  - Phase 1: Enroll two patients to assess safety and tolerability
  - Phase 2: Overall survival at multiple sites (US and Europe) n=7

Primary Outcomes

- Phase 1:
  - Safety associated with treatment
- Phase 2:
  - Survival: proportion of patients alive at age 2 and at least 1-year post infusion (without HSCT)
  - Safety associated with treatment

Secondary Outcomes

- Percentage of patients with at least 10% neutrophil CD18 expression
- Percentage of patients with at least 0.1 peripheral WBC gene marking (VCN) at 6 months post-infusion
- Incidence and severity of infections
- Improvement in neutrophilia
- Resolution (partial or complete) of any underlying skin rash or periodontal abnormalities

[1]Source: https://clinicaltrials.gov/ct2/show/NCT03812263?cond=Leukocyte+Adhesion+Deficiency&rank=5

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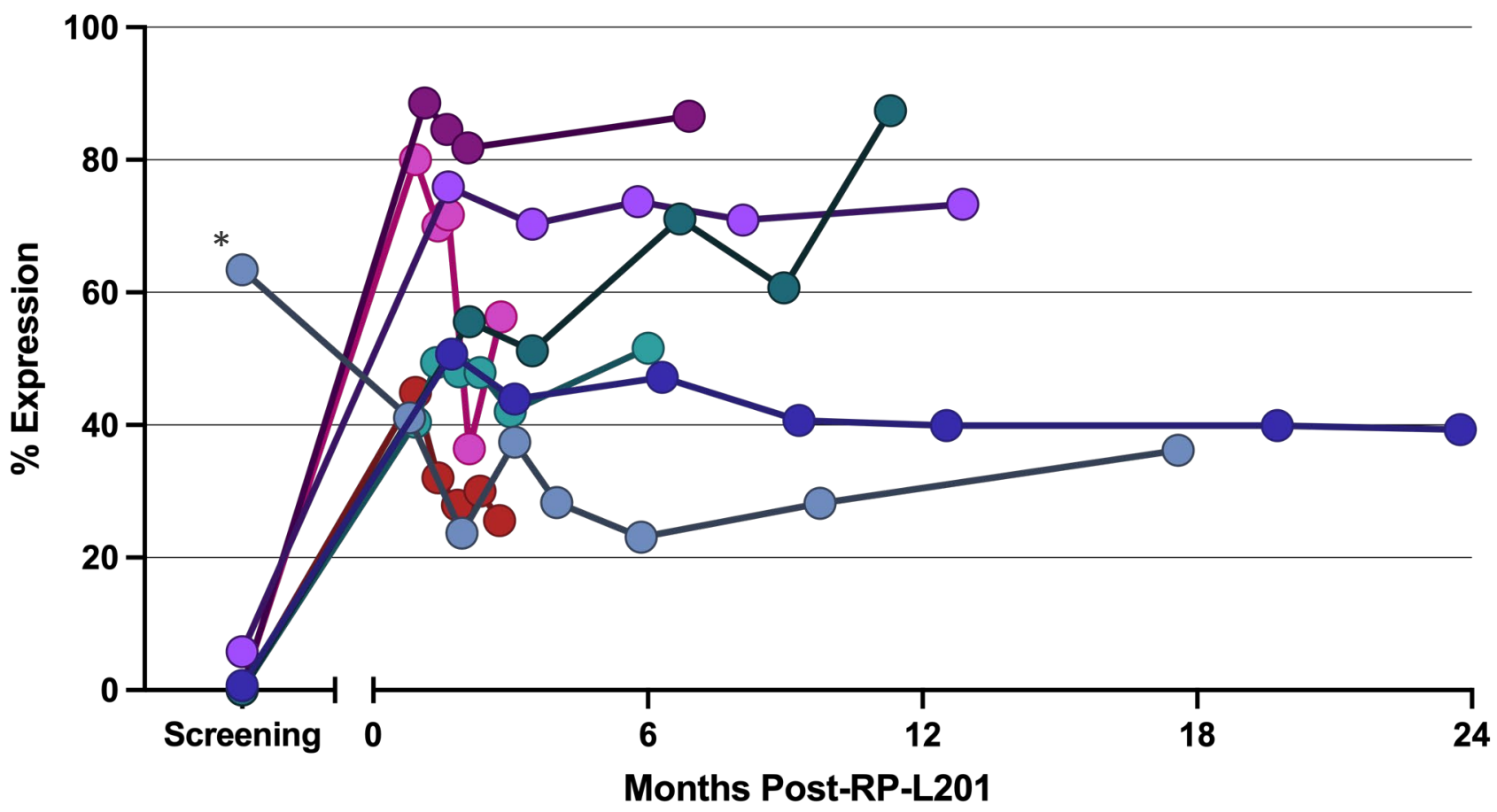
RP-L201: Subject and Cell Product Characteristics

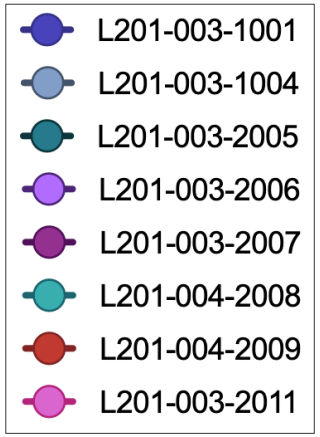
Patient ID	Gender	Age (enrollment)	Drug Product VCN	CD34+ Cell Dose
1 (1001)	F	9 yrs.	3.8	4.2×10^6 cells/kg
2 (1004)	F	3 yrs.	2.5	2.8×10^6 cells/kg
3 (2005)	F	3 yrs.	1.8	6.5×10^6 cells/kg
4 (2006)	M	7 mo.	2.9	4.3×10^6 cells/kg
5 (2007)	M	3 mo.	3.6	5.0×10^6 cells/kg
6 (2008)	M	5 mo.	3.8	3.3×10^6 cells/kg
7 (2009)	M	3 yrs.	2.0	4.5×10^6 cells/kg
8 (2011)	F	2 yrs.	3.8	3.8×10^6 cells/kg
9 (2010)*	F	4 yrs.	3.5	10×10^6 cells/kg

Data reported from 8 of 9 patients; 3–24m follow-up.
*Recent RP-L201 infusion

LAD has received CIRM Funding. Data as of December 2021

RP-L201: CD18 Expression in PB Neutrophils

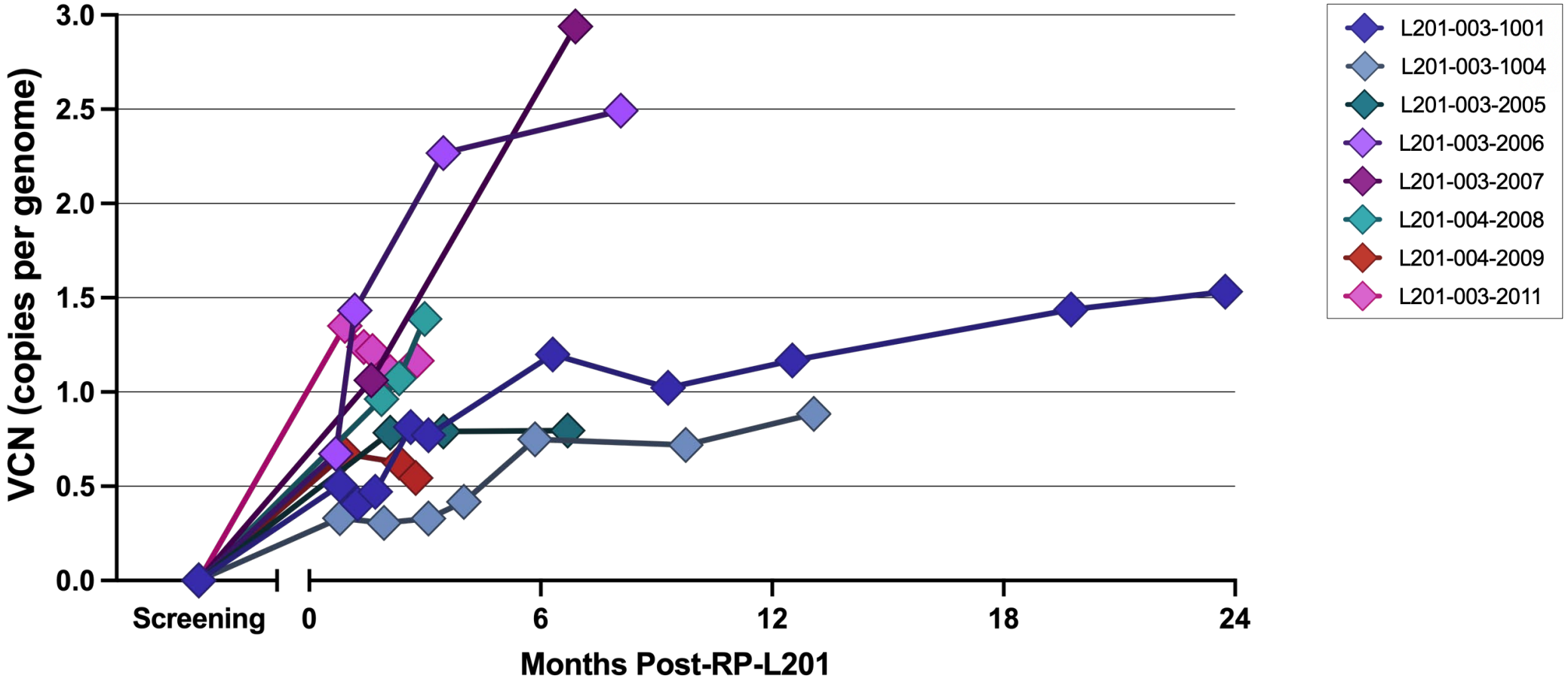




**Dim/weak CD18 expression reported at baseline for PT 1004 in ~60% of Cells*

LAD has received CIRM Funding. Data as of December 2021

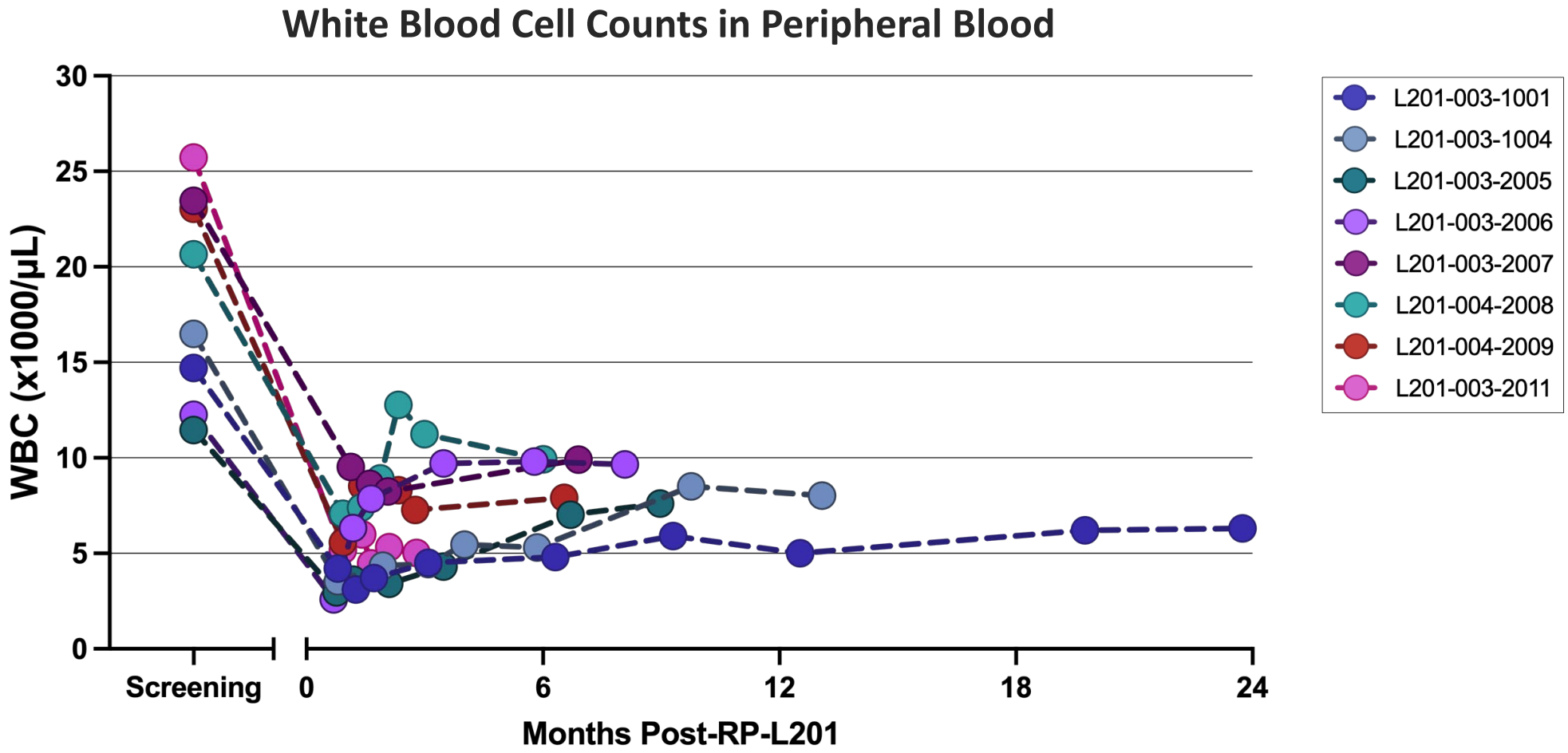
RP-L201: VCN in PBMCs



PBMC: peripheral blood mononuclear cell

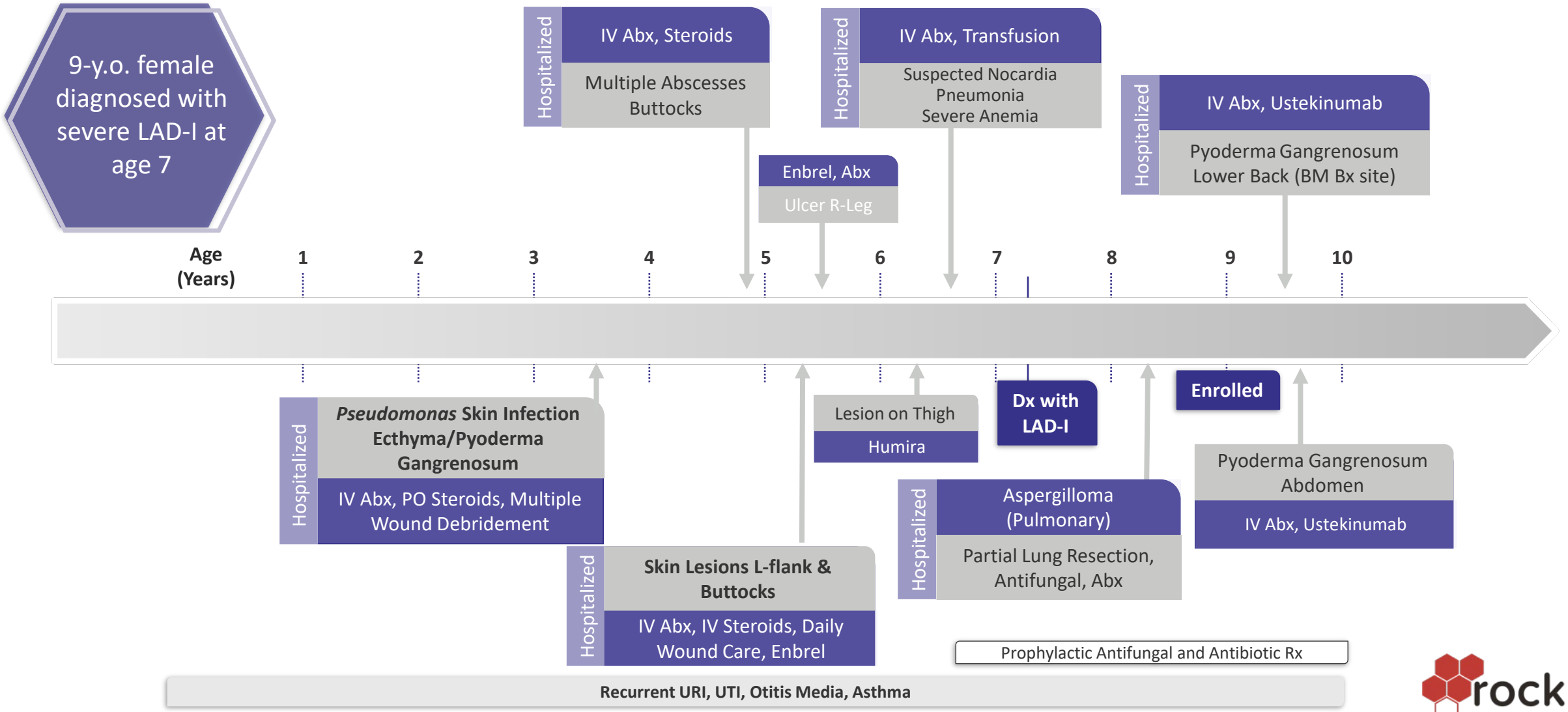
LAD has received CIRM Funding. Data as of December 2021.

RP-L201: Improvements in Leukocytosis Seen Across Patients



LAD has received CIRM Funding. Data as of December 2021.

Pre-Gene Therapy Medical History of Patient 1001



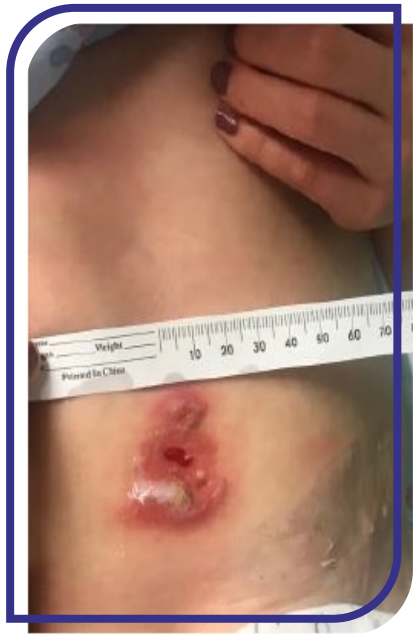
Historical patient records collected by UCLA Mattel Children's Hospital
LAD has received CIRM Funding

Patient 1001: Visible Improvements Post-Treatment

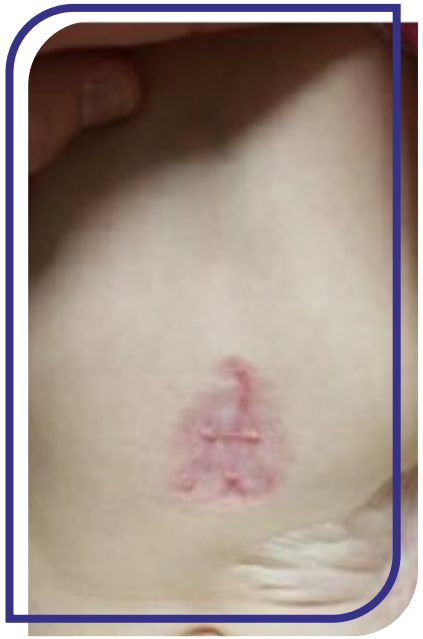
Pre GTx: Severe infections ≥ 1 per year; numerous hospitalizations, severe skin lesions, continuous prophylactic antibiotics and required home schooling

Post GTx: No infections or hospitalizations, off antibiotics and able to attend school

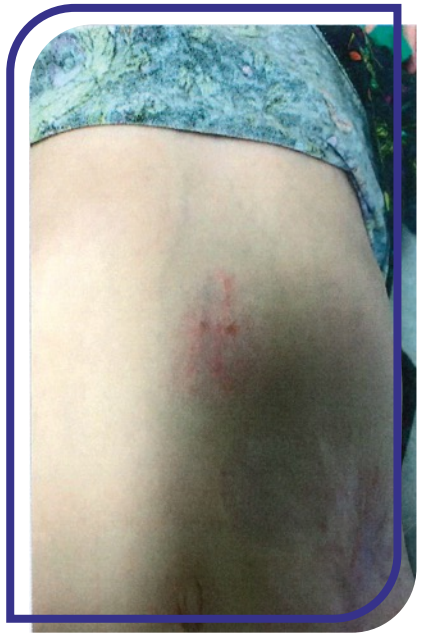
Spontaneous Abdominal Lesion



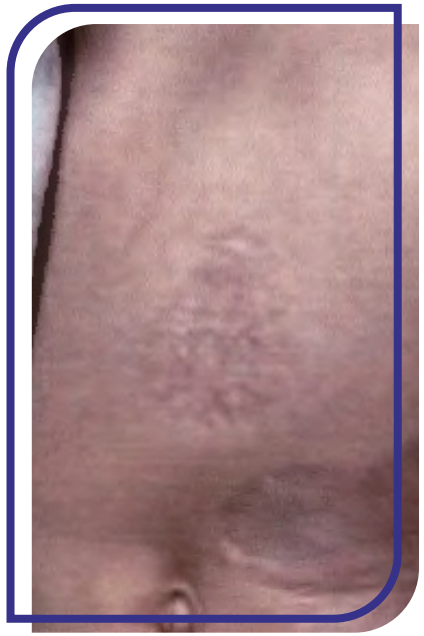
Baseline (Pre-Treatment)



3-months (Post-Treatment)



6-months (Post-Treatment)

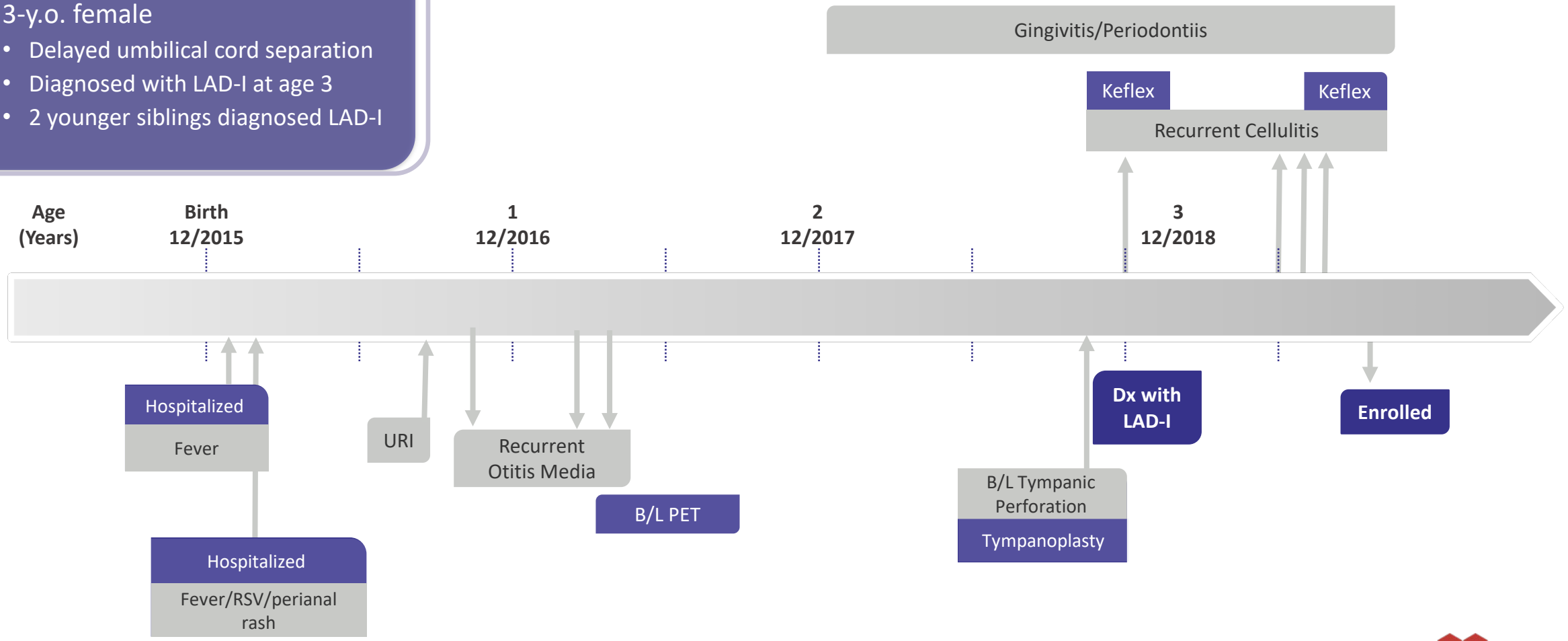


12-months (Post-Treatment)

UCLA Mattel Children's Hospital Data

Pre-Treatment Medical History of Patient 1004

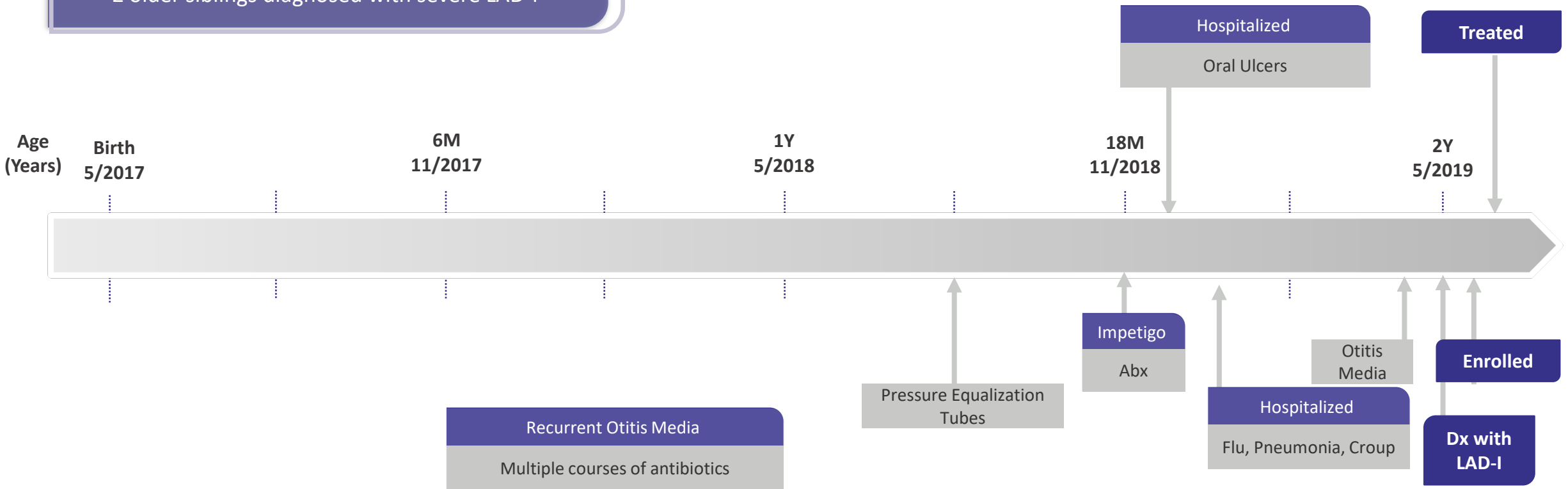
3-y.o. female
- Delayed umbilical cord separation
- Diagnosed with LAD-I at age 3
- 2 younger siblings diagnosed LAD-I



Historical patient records collected by UCLA Mattel Children's Hospital

Pre-Treatment Medical History of Patient 2005

2-y.o. female at enrollment
- Diagnosed with LAD-I at age 2
- 2 older siblings diagnosed with severe LAD-I



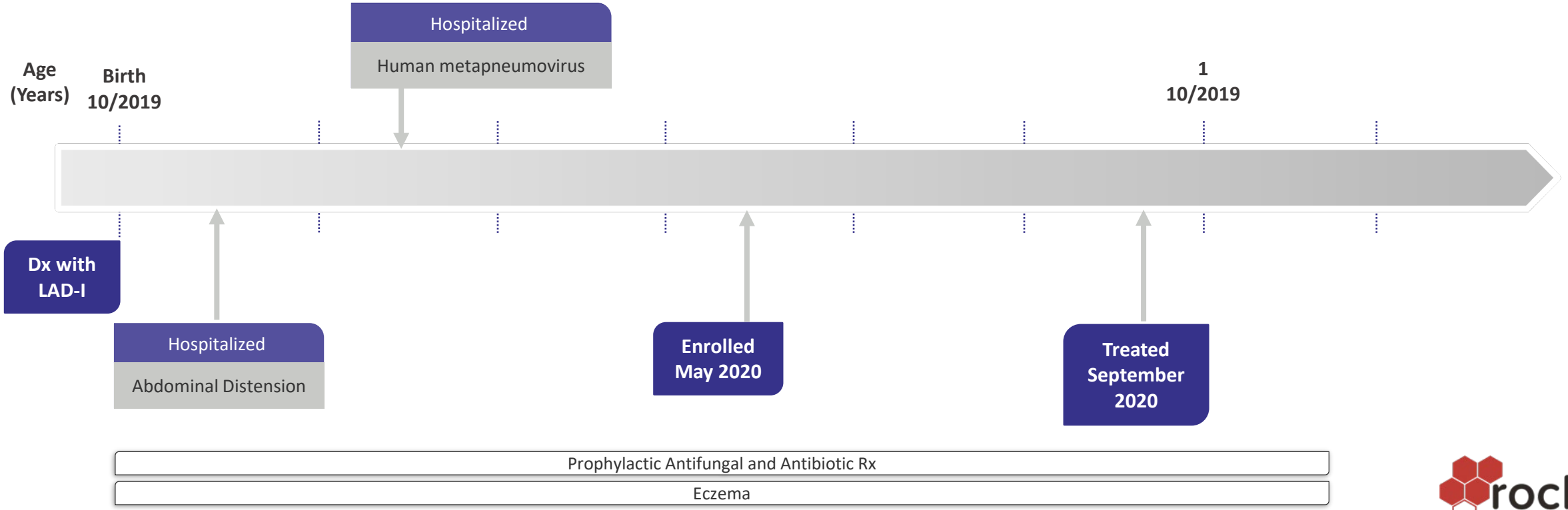
Recurrent viral infections (including hand, foot and mouth disease)
Bronchiolitis x2

Historical patient records collected by UCLA Mattel Children's Hospital

Pre-Treatment Medical History of Patient 2006

7-m.o. male

- Diagnosed at birth given family history of disease
- Delayed separation of umbilical cord (6 weeks)
- 2 older siblings diagnosed with severe LAD-I



Historical patient records collected by UCLA Mattel Children's Hospital

RP-L201 Study Summary

- **Enrollment and dosing complete: 9 of 9 severe LAD-1 patients successfully dosed with RP-L201**
- **Safety profile of RP-L201 appears favorable:**
  - Infusion well tolerated; no drug product-related SAEs or severe Aes
  - Neutrophil engraftment achieved in all subjects in <34 days post-infusion
- **Efficacy evident in 8 of 8 severe LAD-I patients with at least 3-months of follow-up (range 3-24m)**
  - Includes 4 patients with ≥ 12-months of follow-up
  - Patient 1001 with durable CD18+ PMN expression of ~40% and PB VCN of 1.53 at 24-months post-infusion and resolution of pre-existing skin lesions
  - Patient 1004 with CD18+ PMN expression at ~36% 18-months post-infusion and PB VCN of 0.88 at 12-months post-treatment
  - Patient 2006 with CD18+ PMN expression at ~73% 12-months post-infusion and PB VCN of 2.49 at 9-months post-treatment
  - Patient 2005 with CD18+ PMN expression at ~87 12-months post-infusion and PB VCN of 0.80 at 6-months post-treatment
  - All 8 patients have CD18 expression and VCN consistent with reversal of severe LAD-I phenotype.
  - **No LAD-1 related hospitalizations for any of the 8 patients following RP-L201 gene therapy**
- Commercial-grade drug product and centralized testing for all patients treated

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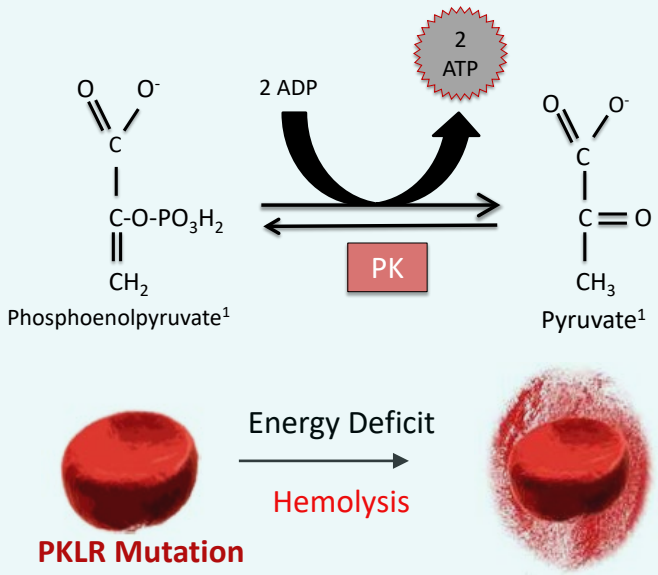
Pyruvate Kinase Deficiency (PKD)
Monogenic Red Blood Cell Hemolytic Disorder

RP-L102	RP-A501	RP-L201	**RP-L301**	RP-L401
Fanconi Anemia	Danon Disease	Leukocyte Adhesion Deficiency-I	Pyruvate Kinase Deficiency	Infantile Malignant Osteopetrosis

OVERVIEW:



- **Current Available Treatments:** ***Chronic*** blood transfusions and splenectomy—side effects include iron overload and extensive ***end-organ damage***
- **Addressable Market[2]:** ***~250-500*** patients/year
- Conservative estimates conclude a number from ***3,000*** to ***8,000*** in the US + Europe combined
- **RP-L301:** ***Improvements in multiple disease components*** in a PKD mouse model, including increased hemoglobin, reduced reticulocytosis, resolved splenomegaly and reduced hepatic erythroid clusters and iron deposits

Regulatory Designations: Fast Track in the US and Orphan Drug designation in the US/EU

[1]One glucose molecule is metabolized into two Phosphoenolpyruvate and ultimately two Pyruvate (pyruvic acid) molecules; this final enzymatic step yields two additional ATPs from each glucose molecule
[2]Market research indicates the application of gene therapy to broader populations could increase the annual market opportunity from approximately 250 to 500, based on an estimated prevalence in the US/EU of approximately 3,000 to 8,000.

Preclinical Studies Demonstrated Safety and Efficacy of Lentiviral-mediated Gene Therapy

PKD mice transplanted with gene-corrected cells demonstrated phenotypic correction:

- Significant increase in RBC count and half-life
- Decreased erythropoietin levels
- Normalized spleen and liver size & structure, with no evidence of erythroid clusters or iron deposits
- Improvement in red cell pyruvate kinase enzymatic pathway as assessed by metabolomic assays

Favorable Safety Results:

- No physical, behavioral biochemical, hematologic or morphologic abnormalities observed in transplanted mice
- Limited evidence of PGK-coRPK-WPRE in nonhematopoietic organs, indicating very low risk of germline transmission
- No evidence of replication competent lentivirus (RCL)

Garcia-Gomez et al. 2016; 24(7): 1187 -1198
Min-Oo, et al. Nat Gene. 2003; 35(4): 357-362.
Min-Oo, et al. Genes Immun. 2004; 5(3): 168-175.

RP-L301: Global Phase 1 PKD Gene Therapy Study

Primary Endpoint

Safety and toxicity of RP-L301

Key Secondary Endpoints

- Clinically significant reduction of anemia
- ***Transfusion independence*** (when relevant) at 12-months
- Achievement of 50% reduction in transfusion requirements (when relevant) at 12-months
- ***PB and BM*** genetic correction as demonstrated by VCN
- Reduction of hemolysis

Key Eligibility Criteria

Inclusion:

- PKD diagnosis with a confirmed *PKLR* mutation
- Age:
  - 1st cohort (N=2): ≥18 to 50-years
  - 2nd cohort (N=2): ≥12 to 17-years
  - 3rd cohort (N=2): ≥ 8 to 11-years
- ***Severe and/or transfusion-dependent anemia***
- Prior splenectomy
- Adequate cardiac, pulmonary, renal and hepatic function

Clinical Sites:

- Hospital Universitario Fundación Jiménez Díaz, Madrid
- Stanford University, Palo Alto, California
- Hospital Infantil Universitario Niño Jesús, Madrid

RP-L301: Patient Characteristics and Product Metrics

Patient Characteristics

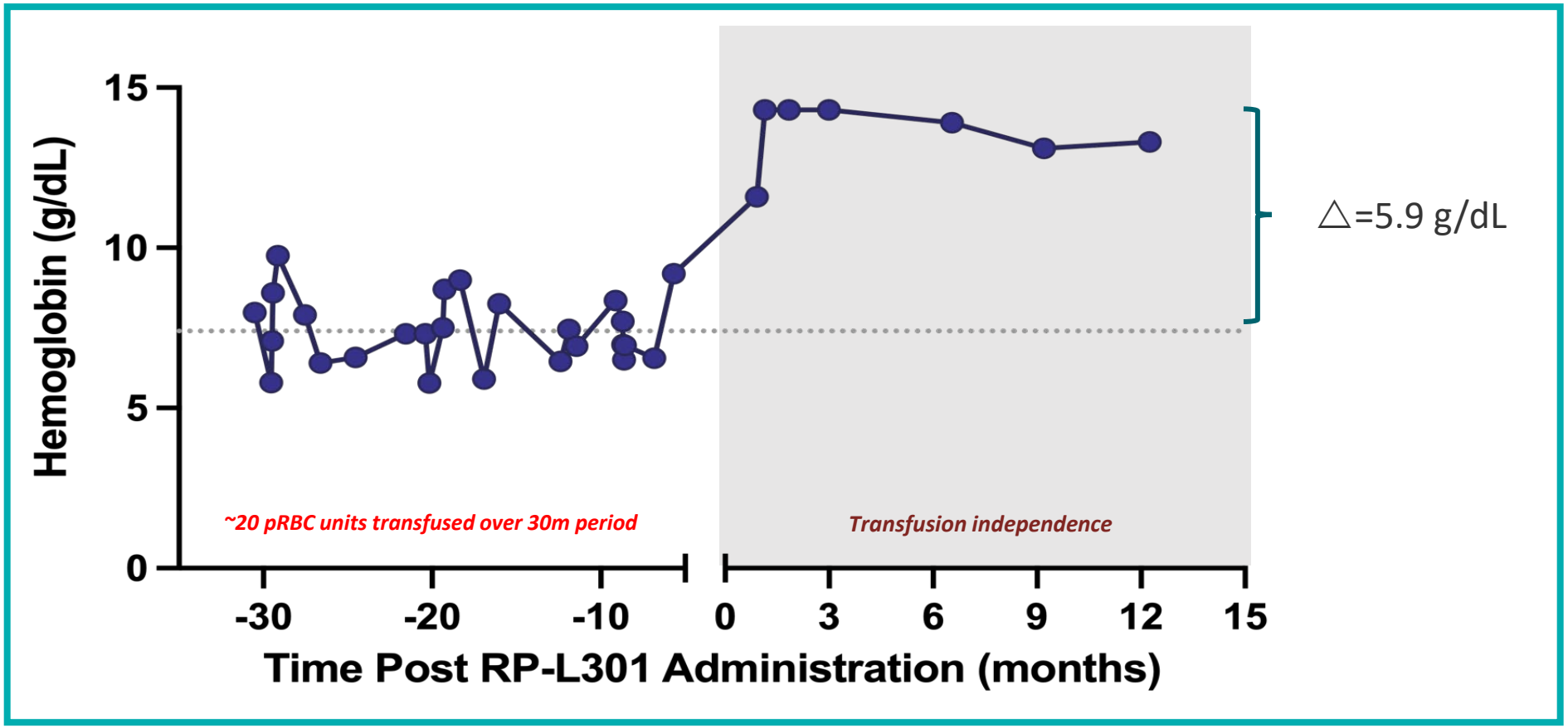
Patient	Age (y) and Gender	Hemoglobin (g/dL)	Bilirubin (mg/dL)	Erythropoietin (mIU/mL)	Transfusion Requirement for 2 Years Prior to Enrollment
1001	31 F	7.4†	13.4 mg/dL	35.6 mIU/mL	~14 transfusion episodes
1002	47 M	7.0‡	7.4 mg/dL	57.2 mIU/mL	~5 transfusion episodes

Product Metrics

Patient	CD34+ Cells/kg	Mean VCN: Liquid Culture
1001	3.9×10^6	2.73
1002	2.4×10^6	2.08

† Average hemoglobin calculated over 2-years prior to study enrollment
‡ Average hemoglobin calculated over 2-years prior to study enrollment; patient has declined red blood cell transfusions

RP-L301: Preliminary Efficacy Results—Patient 1001



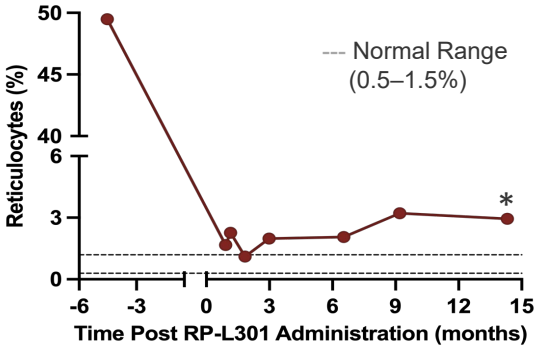
- Marked hemoglobin improvement ~7.4 g/dL to 13.3 g/dL (sustained at 12 months post-infusion)
- No transfusion requirements following engraftment

Note: Lab Values during mobilization/apheresis & post-conditioning period were not included

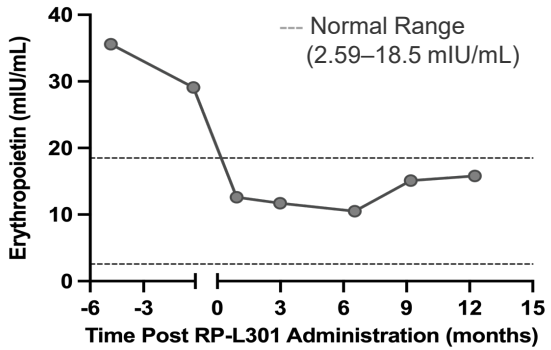
Data as of December 2021

RP-L301: Preliminary Efficacy Results—Patient 1001

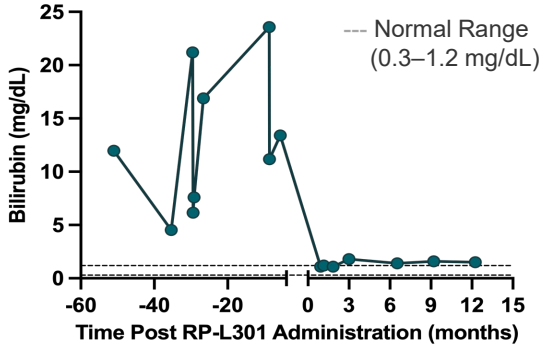
At 1-12 months post RP-L301



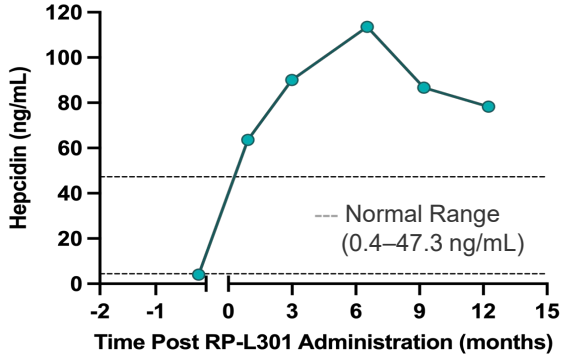
Sustained reduction in reticulocytes



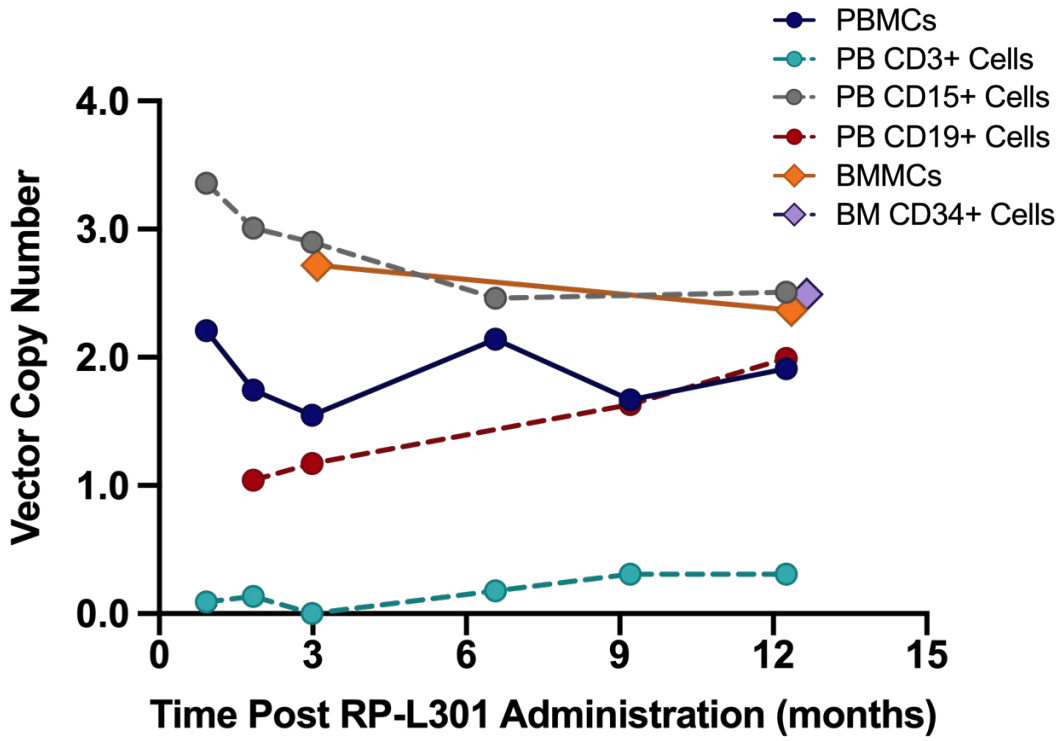
Erythropoietin normalized



Bilirubin decreased from 13.4 mg/dL to 1.5 mg/dL



Hepcidin increased from <4.0 ng/mL to 78.3 ng/mL



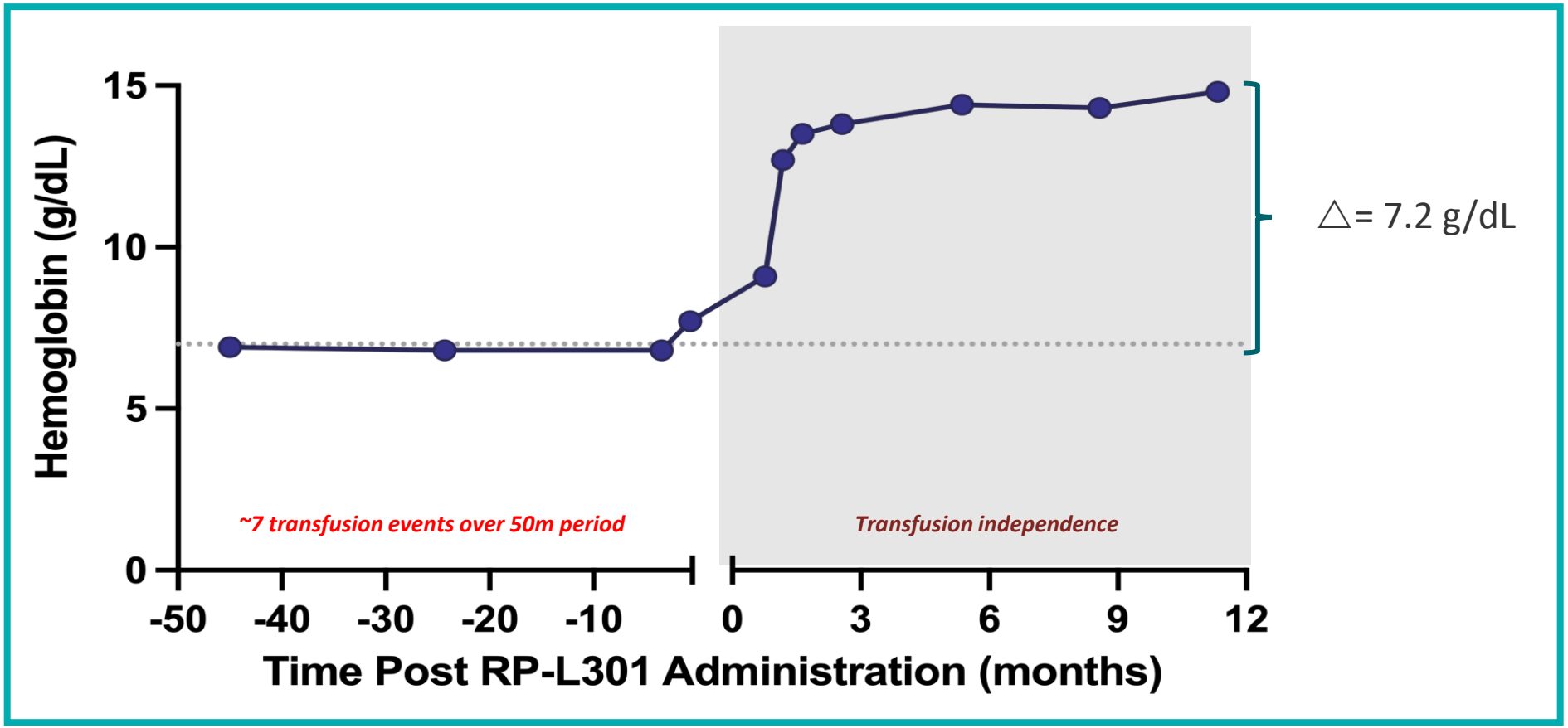
Stable VCN in PBMCs of 1.91 at 12 months and VCN in BMMCs 2.37 at 12 months post RP-L301

Note: Lab Values during mobilization/apheresis & post-conditioning period were not included.

** Reticulocytes not obtained at 12-month visit; obtained locally at ~14 months post-infusion

Data as of December 2021

RP-L301: Preliminary Efficacy Results—Patient 1002



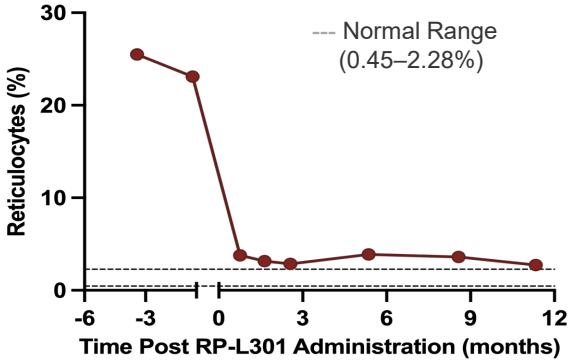
- Hemoglobin normalized to 14.8 g/dL at ~12 months post-rx
- No red blood cell transfusion requirements following engraftment

Note: Lab Values during mobilization/apheresis & post-conditioning period were not included

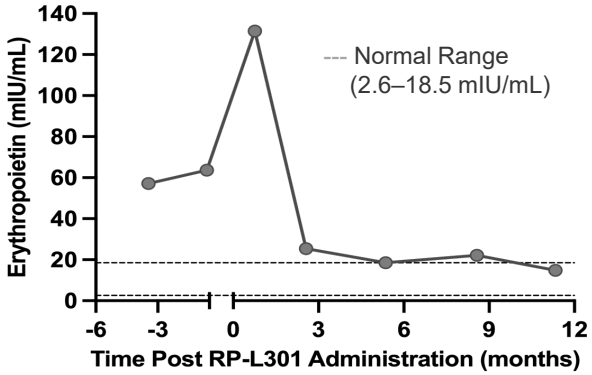
Data as of December 2021

RP-L301: Preliminary Efficacy Results—Patient 1002

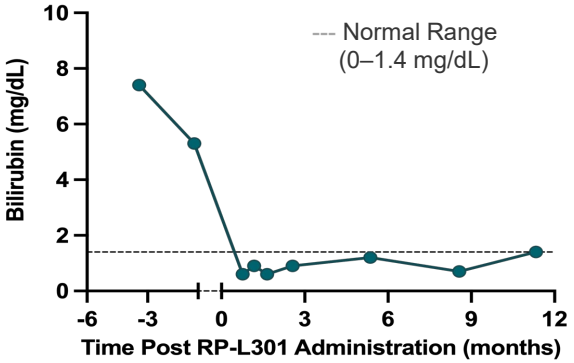
At 1-12 months post RP-L301



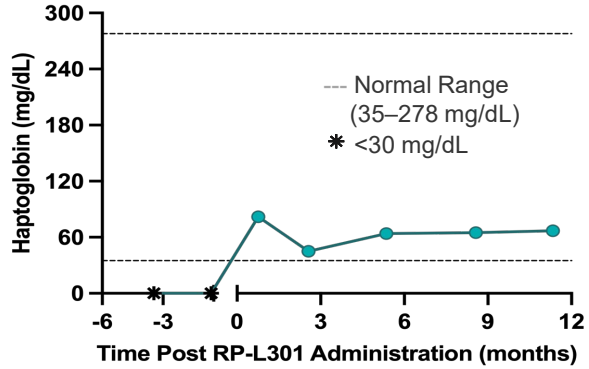
Significant improvement in reticulocytes from 25.5% to 2.73%



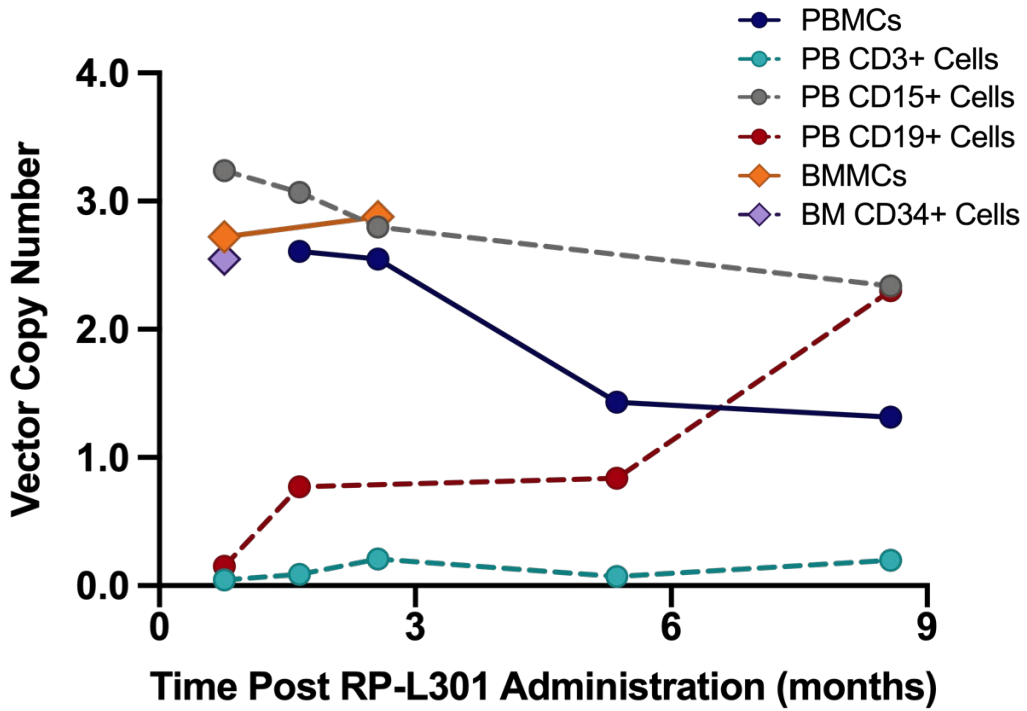
Significant decrease in erythropoietin levels



Normalized bilirubin from 7.4 mg/dL to 1.4 mg/dL



Sustained haptoglobin normalization



Stable VCN in PBMCs of 1.31 at 9 months and VCN in BMMCs 2.88 at 3 months post RP-L301

Note: Lab Values during mobilization/apheresis & post-conditioning period were not included.

* Lab Values during mobilization/apheresis & post-conditioning period were not included.

Data as of December 2021

RP-L301 Conclusion: Sustained Efficacy in First 2 Patients at 1 Year

- Safety profile of RP-L301 ***appears favorable***
  - Infusion well tolerated in (N=2); no IP-related serious adverse events (SAEs) through
    12-months post- infusion in adult patients
  - Hematopoietic reconstitution in less than 2 weeks
  - Patients discharged from hospital within ~1 month following RP-L301 infusion
- Preliminary efficacy activity observed within initial 3-months after administration of RP-L301 and sustained through 12-month visits
  - Both patients have normalized hemoglobin and improving hemolysis markers
  - ***No red blood cell transfusion requirements post-engraftment***
  - Clinical improvement is associated with evidence of engraftment as measured by peripheral blood and bone mVCN
- ***Commercial-grade drug product and centralized testing for all treated patients***

rocket pharma

Infantile Malignant Osteopetrosis (IMO)
Monogenic bone resorption disorder

RP-L102
Fanconi Anemia

RP-A501
Danon Disease

RP-L201
Leukocyte Adhesion Deficiency-I

RP-L301
Pyruvate Kinase Deficiency

RP-L401
Infantile Malignant Osteopetrosis

OVERVIEW:

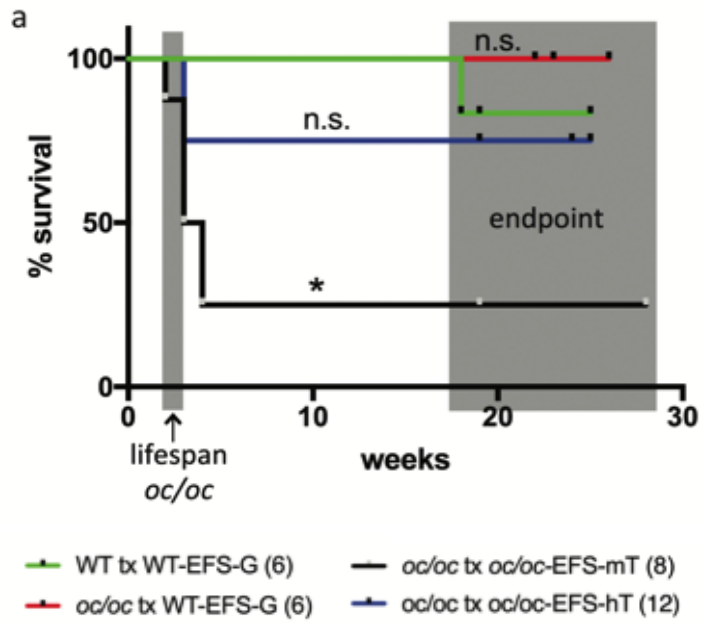
- **Background:** ***Dysfunctional osteoclast*** disease characterized by bone marrow failure, skeletal deformities, and neurologic abnormalities caused by *TCIRG1* mutations in >50% of cases[1]
  - ***Frequent mortality in early years of life, severe marrow failure and visual impairment during 1st year***
- **Current Available Treatments:** Hematopoietic stem cell transplants associated with GVHD and ***limited efficacy***
- **Addressable Market**: ***>50*** patients/year[2]
- **RP-L401:** *In vitro* restoration of osteoclast resorptive function observed; *in vivo* correction in murine model
- **Regulatory Designations:** Rare Pediatric Disease, Orphan Drug and Fast Track designations in the US

[1]Source: https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=667
[2]Estimated incidence of one in 200,000 live births; Source: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=667

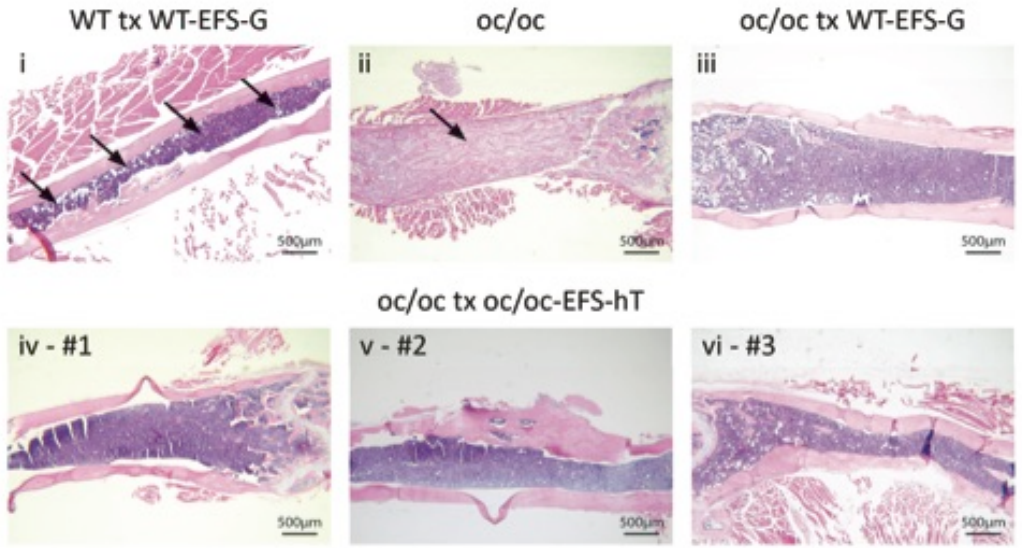
Preclinical Mouse Data Supports Progression to Phase 1

Oc/oc mice receiving RP-L401 showed correction of the disease phenotype, with increased long-term survival, tooth eruption, weight gain, and normalized bone resorption

Increased Long-term Survival



Reversal of Osteopetrotic Bone Phenotype



E-Poster Presented at ESID October 2020

RP-L401 (IMO) Clinical Trial and Outcome Measures[1]

Non-Randomized Phase 1 Study[2]

Design

- Enroll 2 patients, with a confirmed diagnosis of IMO with documented *TCIRG1* mutation
  - 1-month or older

Primary Outcomes

- Safety associated with treatment

Secondary Outcomes

- Normalization of serum calcium and blood counts
- Presence of gene-modified blood and bone marrow cells
- Normalization of bone abnormalities on X-ray and DEXA scans
- Prevention or stabilization of vision and hearing loss
- Reduction in hepatosplenomegaly

1. Phase 1 study enrollment temporarily paused pending a comprehensive evaluation in collaboration with the Independent Data Monitoring Committee, which will include a review of the conditioning regimen and other potential safety measures to mitigate the impact of underlying disease on treatment
2. Source: https://www.clinicaltrials.gov/ct2/show/NCT04525352?term=NCT04525352&draw=2&rank=1

Growing IP Portfolio

Multiple in-licensed patent families for GTx products and related technology platforms

Supporting current pipeline efforts:

- Four In-licensed pending international patent applications filed under Patent Cooperation Treaty (PCT):
  - FA (2)
  - LAD-I
  - PKD
- Multiple patent applications pending:
  - Danon (exclusive world-wide license from UCSD)
- Multiple patent families licensed from REGENXBIO:
  - Danon – AAV9 (exclusive world-wide license)
  - Danon – 2 undisclosed capsid serotypes (exclusive world-wide option to license)
- Multiple cell and gene therapy platform technologies licensed for pipeline product improvements

Rocket Proprietary Filed IP

Extensive patent portfolio across multiple platforms:

- Multiple pending patent applications for ex-vivo LVV programs
- Multiple pending patent applications for in-vivo AAV

World-Class Research and Development Partners

CIBER	IIS FJD	REGENXBIO	University of California, Los Angeles
CIEMAT	Lund University	Stanford Medical School	University of Minnesota
Fred Hutchinson Cancer Research Center	Memorial Sloan Kettering Cancer Center	UCL	University of Pennsylvania
Hospital Universitario Fundación Jiménez Díaz	Niño Jesús Hospital	University of California, San Diego	

Expansion into Cranbury, NJ: R&D/CMC Efforts and Eventual cGMP Manufacturing

2021

- Continue R&D to ***further support*** CMC analytics and internal QC and release testing activities for RP-A501
- 50,000 sq. ft. from this facility will be ***dedicated to AAV cGMP*** manufacturing (FDA and EMA compliant)
- ***In-house*** GMP manufacturing readiness
- Enables ***dual-sourcing*** for Danon commercial capacity

RCKT Cranbury (NJ)
103,720 sq. ft. production facility