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Corporate Presentation

JUNE 2022

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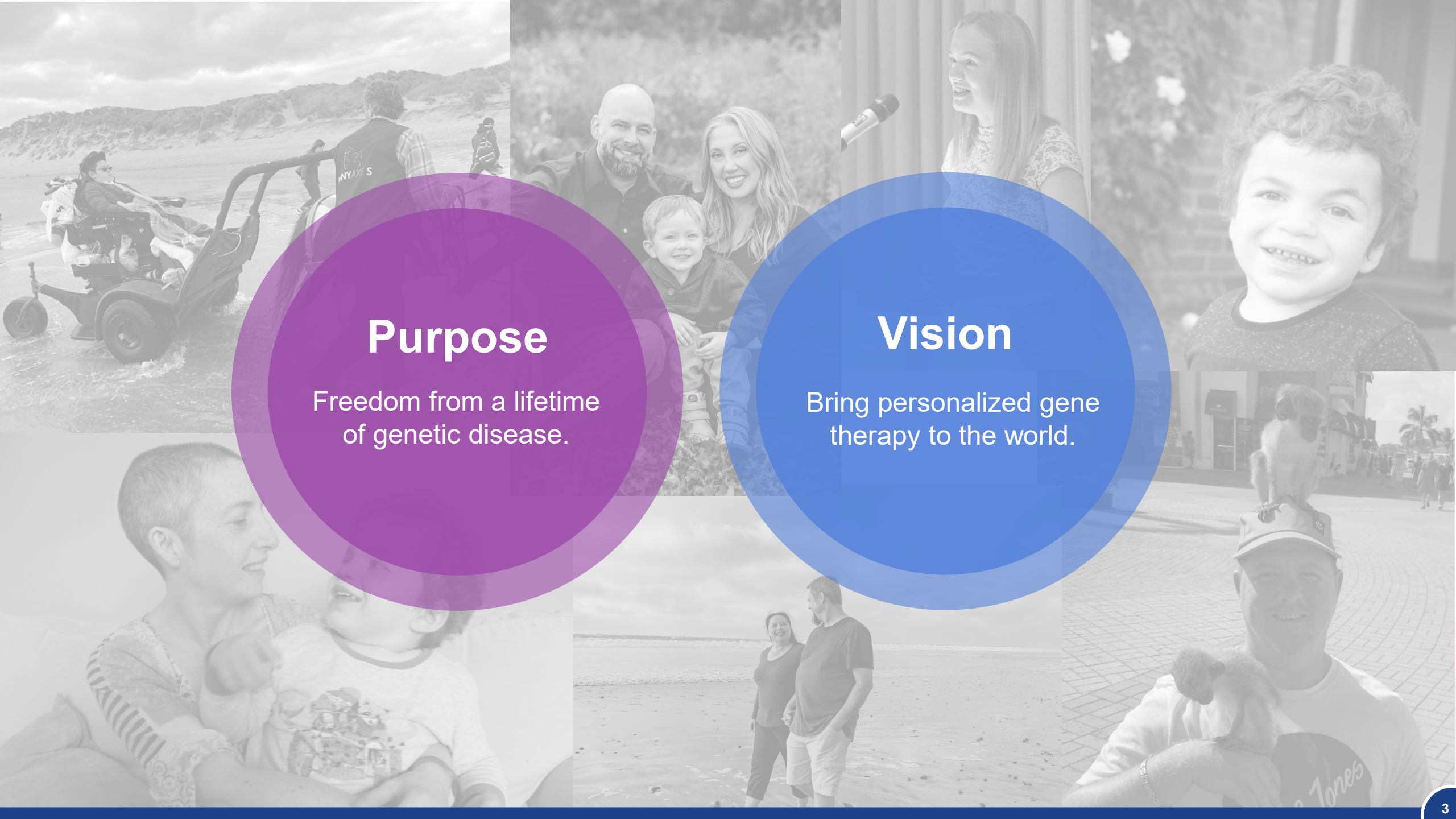

Purpose

Freedom from a lifetime of genetic disease.

Vision

Bring personalized gene therapy to the world.

Investment highlights

- Leading hematopoietic stem cell (HSC) gene therapy company
- Targeting lysosomal disorders representing a multi-billion dollar revenue opportunity
- Strong efficacy and safety profile to date across two clinical-stage programs
- Regulatory discussions planned for 2H 2022 to frame approval pathways for multiple indications
- Strong balance sheet with cash runway into Q1 2024

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Near-term opportunities in leading gene therapy pipeline

Potential billion-dollar revenue opportunities

AVR-RD-04 for cystinosis

- First and only gene therapy for cystinosis in clinic
- Proof-of-concept demonstrated in adults
- Secured U.S./EU Orphan Disease Designation and U.S. Fast Track Designation

- Plan to meet with regulators in 2H 2022 to discuss company-sponsored trial
- Plan to initiate company-sponsored trial in 2023

AVR-RD-02* for Gaucher disease type 3

- Second program in Gaucher disease franchise
- Leverages clinical and CMC work conducted in Gaucher disease type 1, which was first gene therapy for Gaucher to enter clinical trials

- Plan to engage with regulators on potential Phase 2/3 trial in 2H 2022
- Plan to initiate potential Phase 2/3 trial in 2023

Other anticipated 2022 catalysts:

- AVR-RD-02 for Gaucher disease type 1 – planned clinical update
- AVR-RD-05 for Hunter syndrome – CTA authorization expected
- AVR-RD-03 for Pompe disease – engage with regulators on clinical trial

*Planned regulatory milestones subject to regulatory agency clearance; * Formerly referred to as AVR-RD-06; collaborator-sponsored Phase 1/2 clinical trial of AVR-RD-04 is funded in part by grants to UCSD from the California Institute for Regenerative Medicine (CIRM), Cystinosis Research Foundation (CRF) and National Institutes of Health (NIH)*

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Multi-billion dollar market opportunity

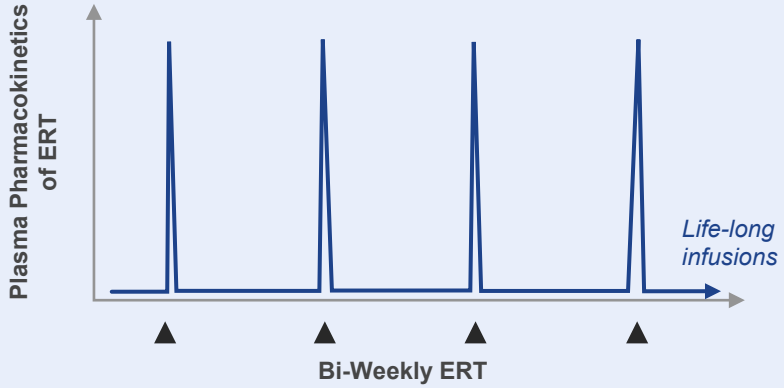
Cost of standard of care in target indications is extremely high

Disease	Approx. 2020 Global Net Sales†	Five-Year SOC Cost per U.S. Patient*	Selected Companies w/ Marketed Therapies
Cystinosis	$0.2B	$4.3M‡	Horizon Pharma
Gaucher	$1.5B	$2.3M	Sanofi Genzyme; Takeda Shire
Hunter	$0.6B	$2.4M	Takeda Shire
Pompe	$1.1B	$3.2M	Sanofi Genzyme
	Total: $3.4B		

*Sources: Rombach S et al., Orphanet J Rare Dis, 2013; van Dussen L et al., Orphanet J Rare Dis, 2014 ; * WAC pricing from Redbook using standard dosing assumptions*
† 2020 Net Sales from company annual and other reports; ‡ Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate), mid point between avg. adult and pediatric
Note: Shire acquired by Takeda in 2019; SOC: Standard of Care

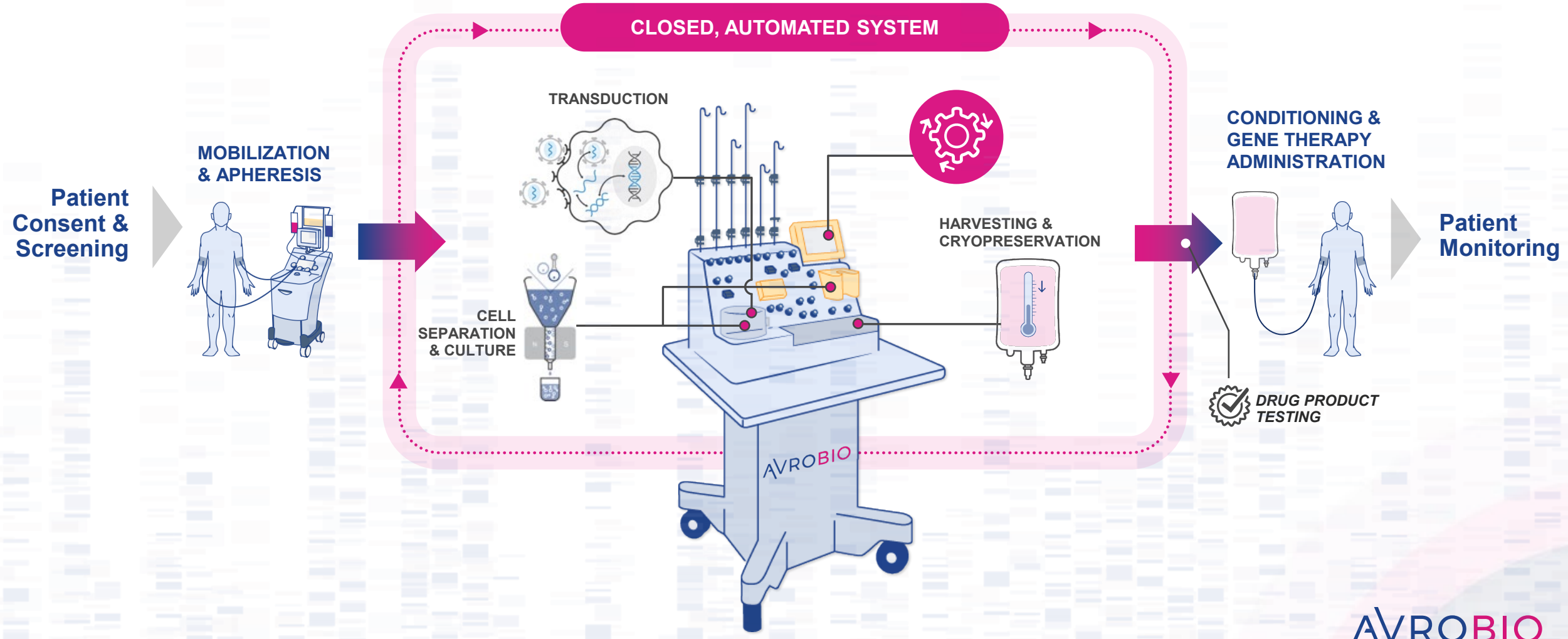
Significant advantages over standard of care

Lifelong treatments vs. potential single-dose therapy

	DISEASE PROGRESSION CONTINUES	COULD HALT, PREVENT OR REVERSE DISEASE
	Enzyme Replacement Therapy (ERT) Temporary bolus of enzyme, not curative  	**AVROBIO Gene Therapy** Designed for 24/7 expression of protein, curative potential 
Enzyme or protein level	Transient, intermittent elevation	Long-term, continuous elevation
Treatment burden	Bi-weekly IV infusions	Single IV infusion
Ability to impact CNS	No	Yes

ERT: Enzyme Replacement Therapy; IV: Intravenous; HSC: Hematopoietic Stem Cells

Unrivaled commercial-scale platform in plato®



Cystinosis

Cystinosis opportunity

Standard of care (SOC): Cysteamine pills & eye drops

- Not curative, relentless progression of disease continues; significantly shortened lifespan; kidney transplant often required
- Substantial side effects (e.g., halitosis and GI disturbances), resulting in low compliance and poor quality of life
- Burdensome and expensive – high pill burden and frequent eye drops throughout the day; 5-year treatment cost in the U.S. with SOC ~$4.3 million*

Unmet needs with SOC:

Everyday burden of illness, reduced life expectancy
High pill burden causes GI discomfort; sulfur body odor and breath

Endocrine disorders
Softening & deformation of bones, hypothyroidism, diabetes, infertility

Kidney function
Renal Fanconi syndrome, proteinuria, CKD, kidney failure

CNS complications
Myopathy, hypotonia, tremors, swallowing, neurodevelopmental issues

Vision
Corneal cystine accumulation, photophobia, involuntary eyelid closure

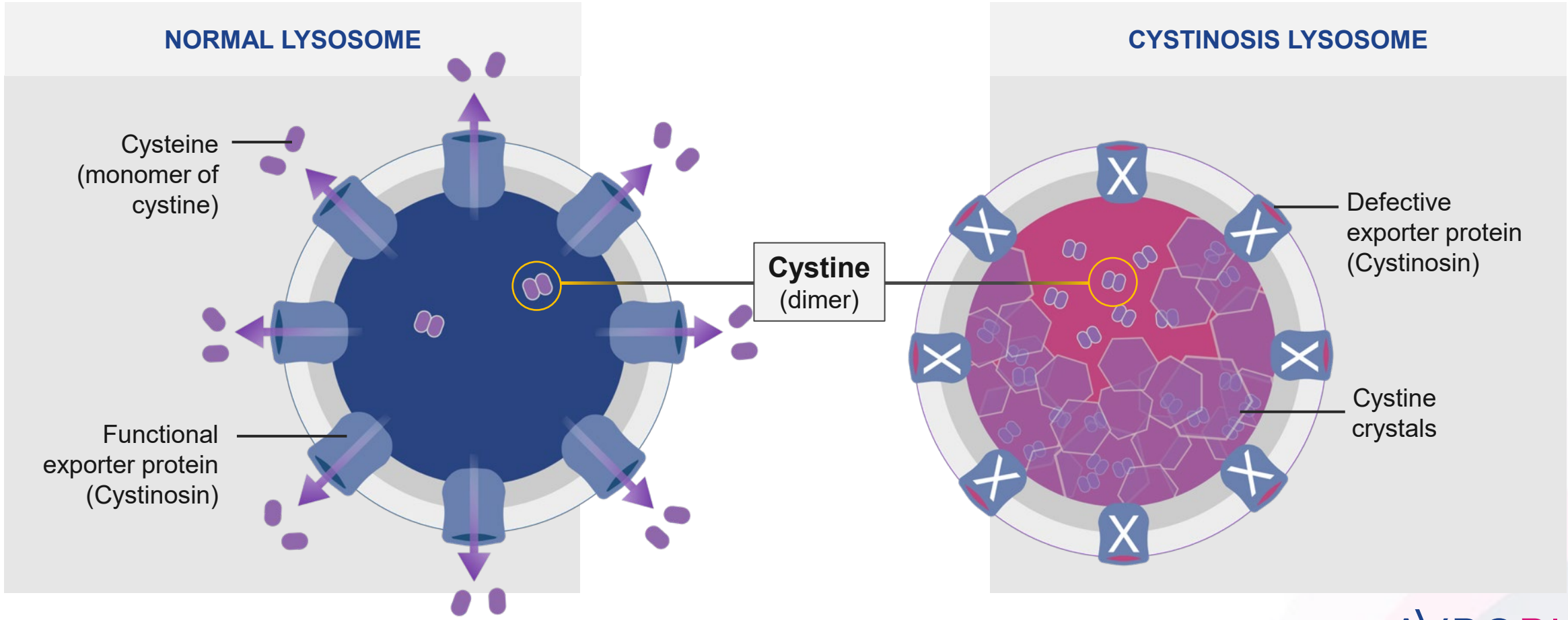
Affects ~ 1:170,000 people

Jaxon, living with cystinosis

WAC pricing from Redbook using standard dosing assumptions. Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate), midpoint between avg. adult and pediatric

Cystinosis caused by defective gene that encodes cystinosin, an exporter protein

Cystine crystals build up in lysosomes causing tissue and organ damage



Source: Cherqui et al, Nat Rev Nephrol. 2017

AVR-RD-04 collaborator-sponsored trial

PHASE 1/2
AVR-RD-04

FULLY ENROLLED:

OBJECTIVES

- Safety and tolerability
- Hypothesis generation of endpoints

PATIENTS

- 6 patients (5 patients dosed to date)
- Adults and adolescents
- Cohorts 1-2 >18 years; Cohort 3 >14 years
- Male and female
- Oral and ophthalmic cysteamine

AVR-RD-04 trial sponsored by University of California, San Diego; does not use plato® platform; AVR-RD-04 aka CTNS-RD-04
Clinical trial funded in part by grants to UCSD from the California Institute for Regenerative Medicine (CIRM), Cystinosis Research Foundation (CRF) and National Institutes of Health (NIH)
All clinical data in this presentation have been provided by the sponsor and are preliminary and subject to change. For open-label studies in which interim reports are provided, the data are regularly reviewed and validated. As a result, certain data may change over time, including reductions or increases in the number of reported safety events, until the database is locked at end of study.

Expanding Phase 1/2 data set shows systemic gene therapy impact

AVR-RD-04 is *first and only* investigational gene therapy for cystinosis

All five patients dosed remain off oral cysteamine

- Improvements in neurocognitive assessments
- Stable muscle/grip strength
- Reduction in cystine crystals in skin and gastrointestinal mucosa
- Improved or stable eye measures
- Reduction in leukocyte cystine to target levels
- Quantified increase in hair strand pigmentation

Safety and tolerability profile remains strong*

Proof-of-concept demonstrated in adult population

Plan to meet with regulators in 2H 2022 to discuss company-sponsored trial

** Data as of May 6, 2022*

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All patients continue to be oral cysteamine-independent

Patient #1 out 2 ½ years

	PATIENT	MONTHS OFF CYSTEAMINE PILLS AND EYE DROPS POST AVR-RD-04 INFUSION	CURRENT STATUS
cysteamine pills	PATIENT 1	31	OFF
	PATIENT 2	22	OFF
	PATIENT 3	17	OFF
	PATIENT 4	5	OFF
	PATIENT 5	1	OFF
cysteamine eye drops	PATIENT 1	31	OFF
	PATIENT 2	13	ON (patient restarted July 2021)
	PATIENT 3	17	OFF
	PATIENT 4	Was not on cysteamine eye drops prior to infusion	OFF
	PATIENT 5	1	OFF

Note: Patients 2, 3 and 5 stopped cysteamine eye drops 1-month post-transplant (per protocol); Patient 1 stopped cysteamine eye drops prior to baseline; Patient 4 was not on cysteamine drops prior to infusion. Data as of May 6, 2022

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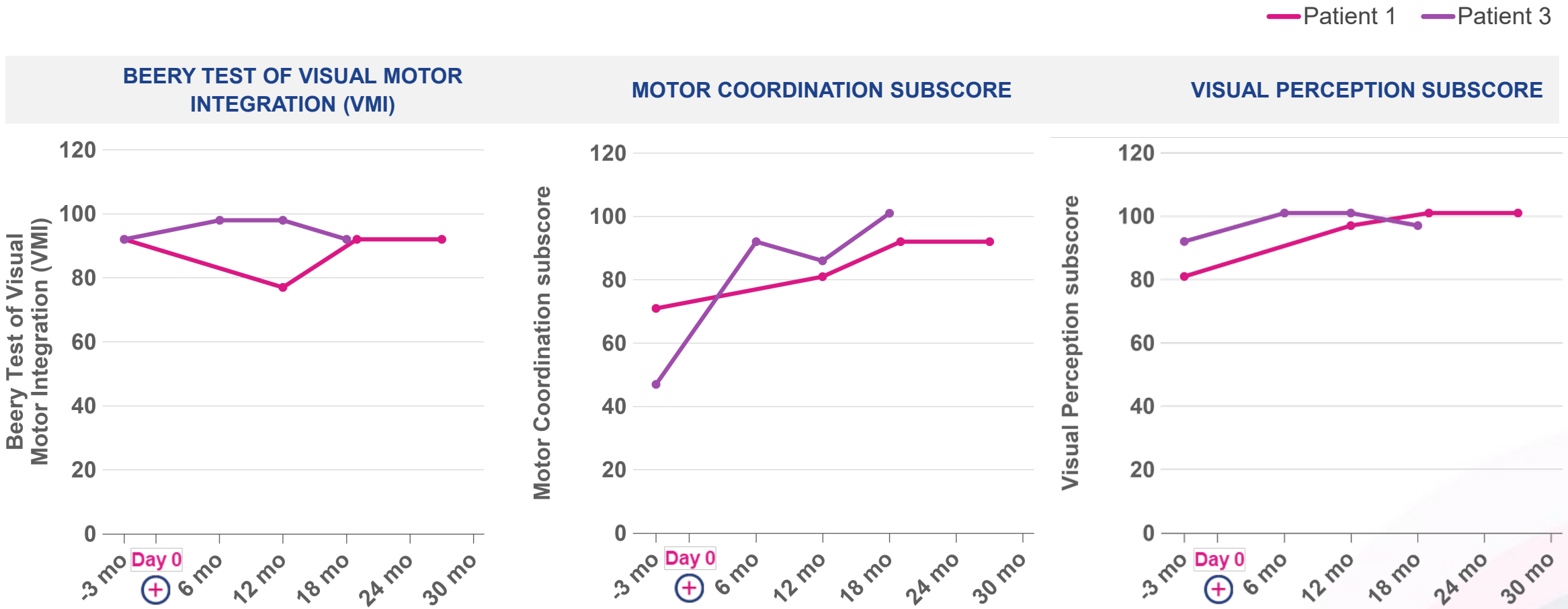
Improvement in motor coordination and visual perception observed post gene therapy



Data for Patient 2 are not available; The Beery – Buktenica Developmental Test of Visual Motor Integration (Beery VMI) is a standardized test evaluating the ability of the brain to interpret and translate visual information into an exact motor response

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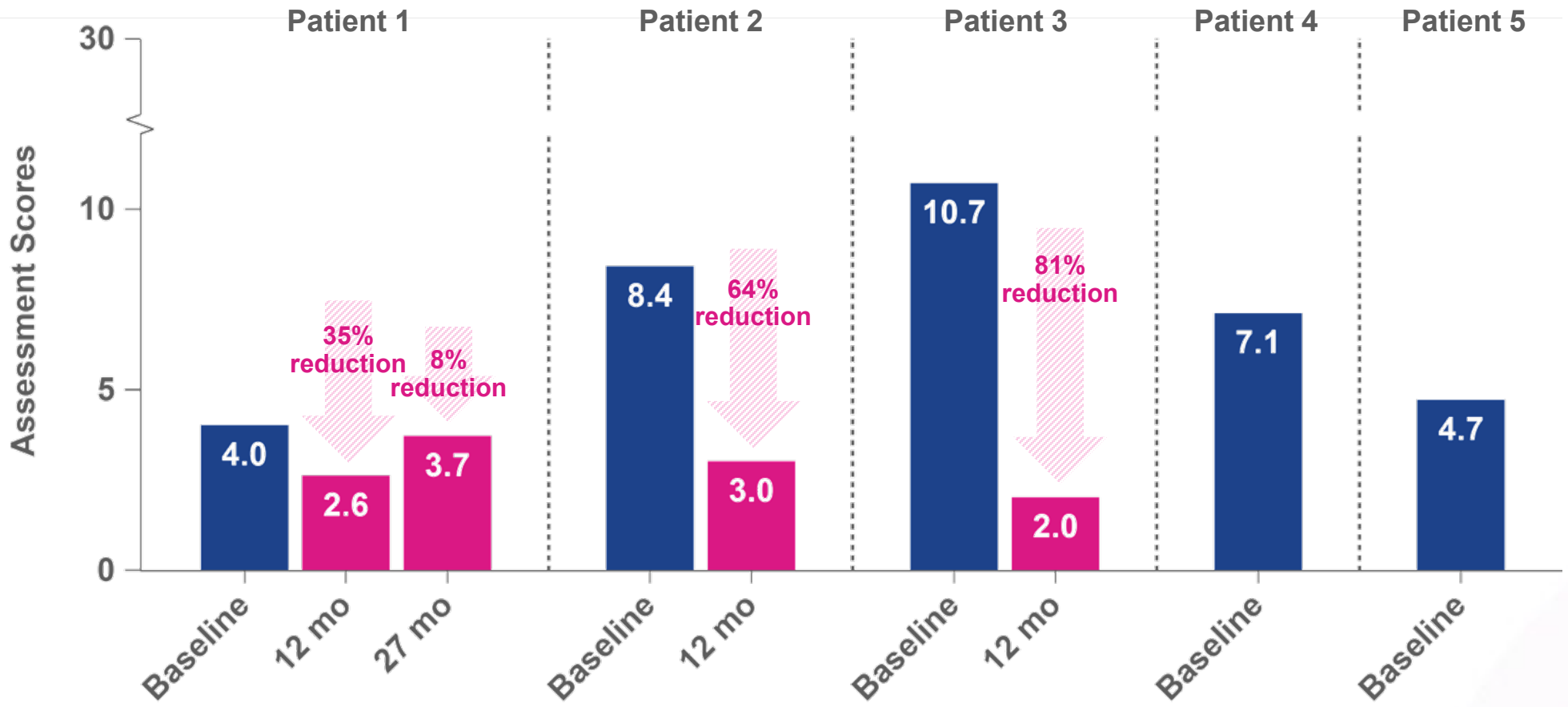
Reduction in number of skin cystine crystals below patients' own SOC baseline at 12+ months

SKIN BIOPSY: AVERAGE INTRACYTOPLASMIC CRYSTALS PER CELL



For Patient 4 and 5, only their Baseline data is currently available

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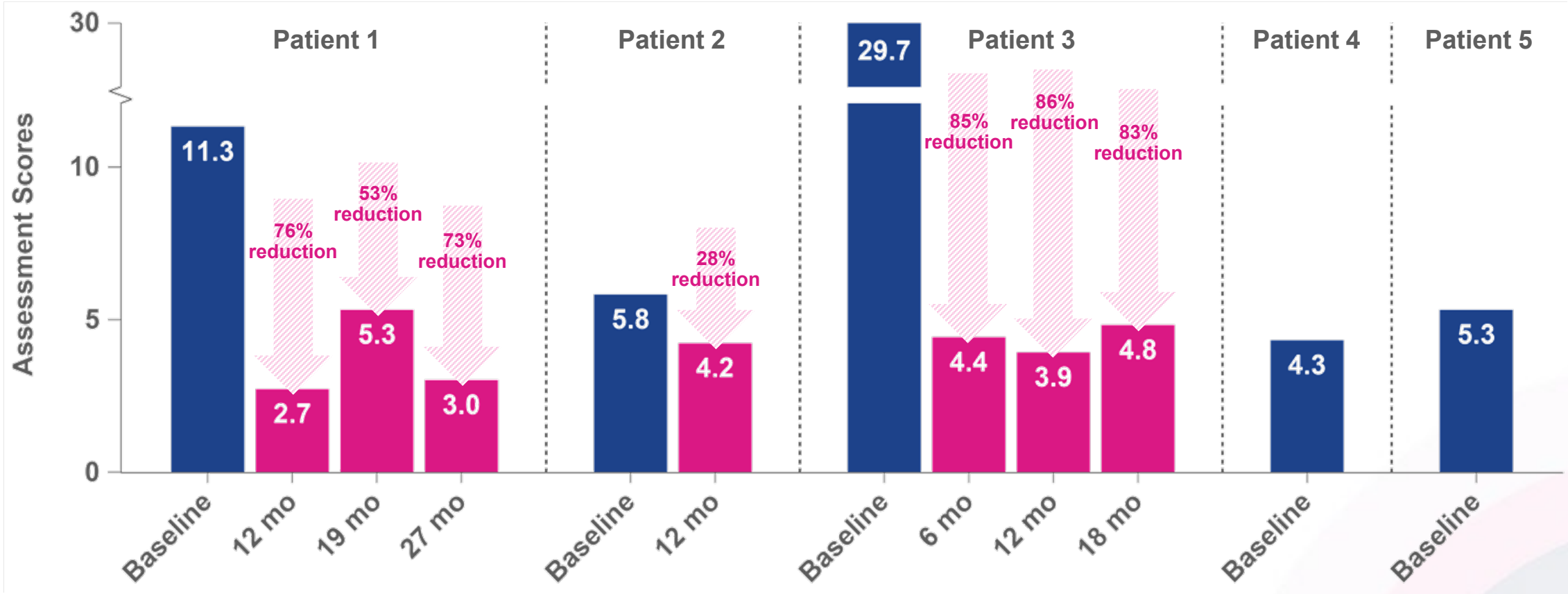
Reduction in number of cystine crystals in gastrointestinal mucosa below patients' own SOC baseline at 12+ months

RECTAL BIOPSY: AVERAGE INTRACYTOPLASMIC CRYSTALS PER CELL

NEW DATA



For Patient 4 and 5, only their Baseline data is currently available

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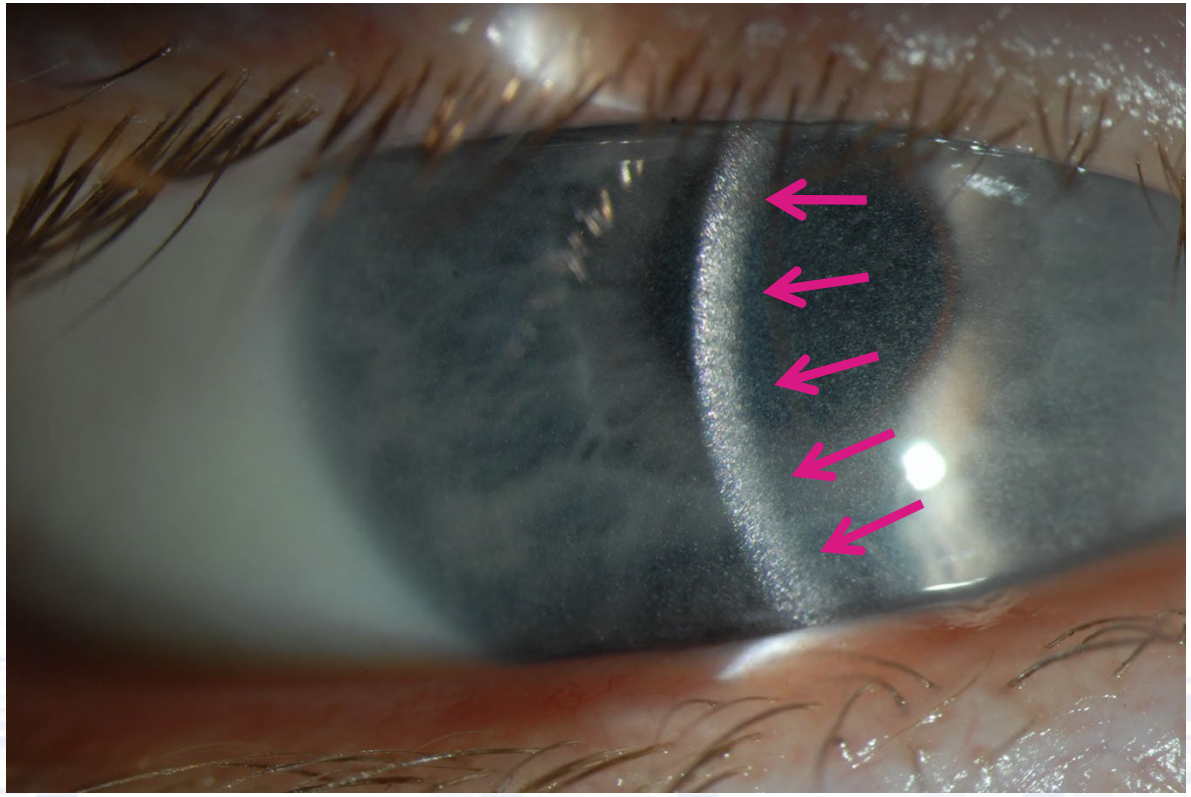
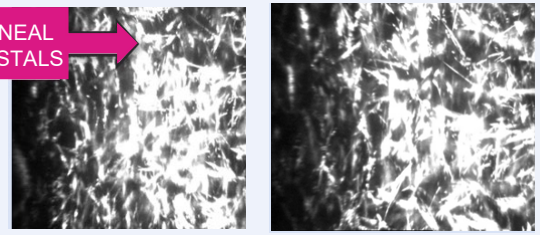
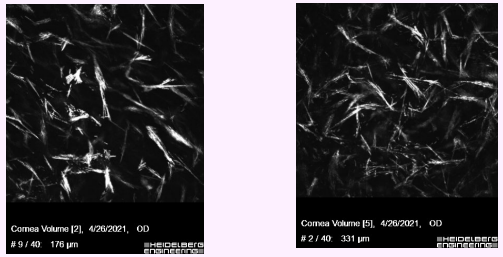
Crystal buildup in eye clearly visible before gene therapy

Treatment goal is to prevent or halt further accumulation of corneal crystals; complete clearance not expected



Patient 1 at baseline

Decline in corneal crystals and improved photophobia grade

	BASELINE		18 MONTHS IMAGES/24 MONTHS PHOTOPHOBIA GRADE	
	IVCM Images	Photophobia Grade* (patient reported)	IVCM Images	Photophobia Grade* (patient reported)
PATIENT 1	*Front* of Cornea ... *Back* of Cornea CORNEAL CRYSTALS  *174 µm, OD* *331 µm, OD*	3	*Front* of Cornea ... *Back* of Cornea  *176 µm, OD* *331 µm, OD*	1

Eye layers	Right eye		Left eye	
	Baseline	12 months	Baseline	12 months
Anterior Stroma	4	3	4	1.9
Middle Stroma	4	3	4	1.7
Posterior Stroma	4	2.1	4	2

Preliminary scoring performed by Dr. Hong Liang

CNRS, Paris, France

*IVCM: In Vivo Confocal Microscopy; exploratory method; These results are for a single patient only and may vary in the study population; OD: Oculus Dexter (right eye); HRT3: Heidelberg Retina Tomograph 3; Scoring instructions: for each layer, assign a score of 0-4, where 0=no crystal; 1 <25%; 2=25-50%; 3=50-75%; 4>75%; Liang et al., IOVS 2015; * Score range: 1-5 where 1 is no photophobia and 5 is severe; Images obtained for Patient 1 at baseline using Nidek Confoscan and used Heidelberg HRT3 w/ Rostock Corneal Module for all other images*

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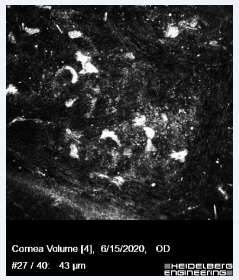
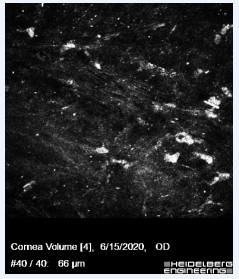
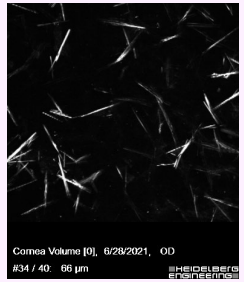
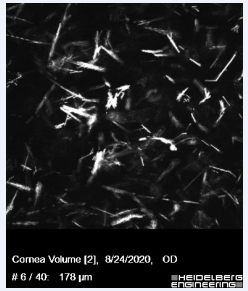
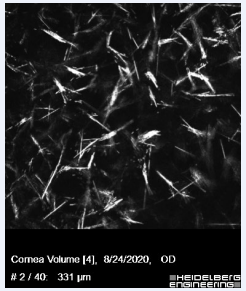
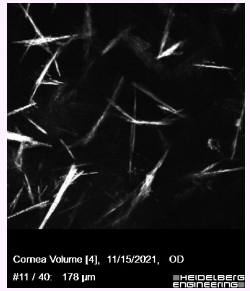
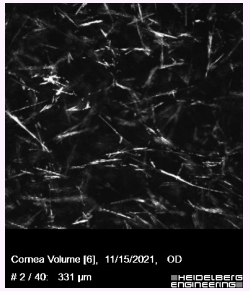
Stable corneal crystals and photophobia grade

	BASELINE		12 MONTHS	
	IVCM Images	Photophobia Grade (patient reported)	IVCM Images	Photophobia Grade (patient reported)
PATIENT 2	*Front* of Cornea:  43 µm, OD *Back* of Cornea:  66 µm, OD	2 or 3	*Front* of Cornea:  43 µm, OD *Back* of Cornea:  66 µm, OD	2
PATIENT 3	 178 µm, OD  331 µm, OD	2	 178 µm, OD  331 µm, OD	2

*IVCM: In Vivo Confocal Microscopy; exploratory method; These results are for a single patient only and may vary in the study population; OD: Oculus Dexter (right eye); HRT3: Heidelberg Retina Tomograph 3; Scoring instructions: for each layer, assign a score of 0-4, where 0=no crystal; 1 <25%; 2=25-50%; 3=50-75%; 4>75%; Liang et al., IOVS 2015; * Score range: 1-5 where 1 is no photophobia and 5 is severe;*

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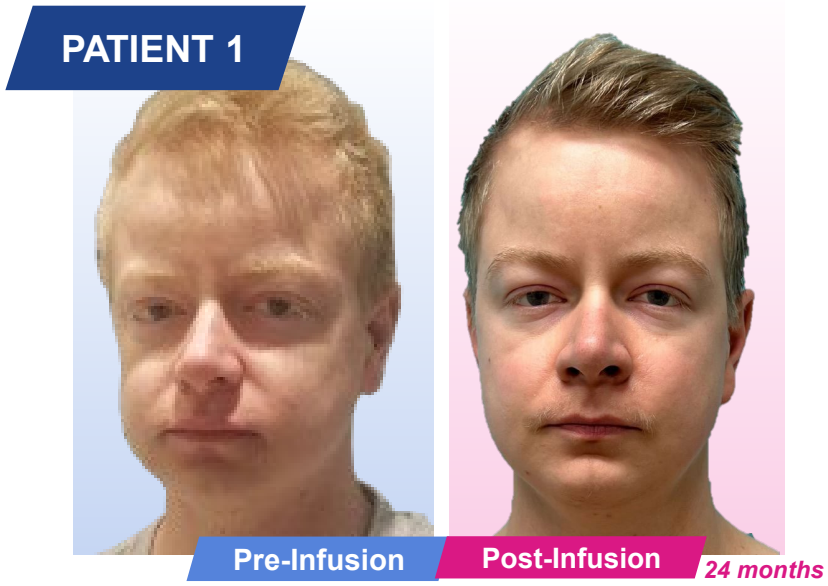
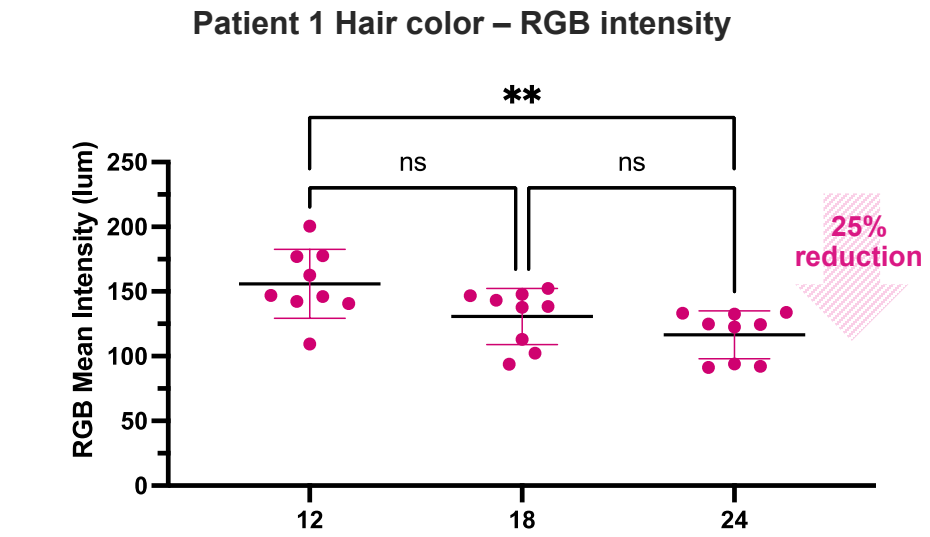
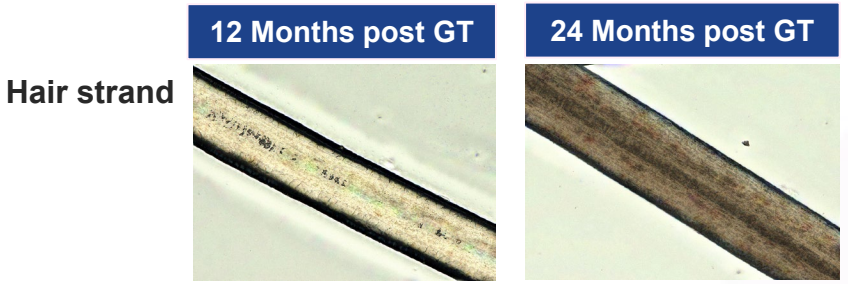
Darker pigmentation may be a sign of multi-functional cystinosin activity post gene therapy

Further enforces systemic reach of gene therapy

Cystinosin is located in melanosomes and regulates melanin synthesis







Note: GT: gene therapy; Source: Chiaverini et al., FESEB, 2012

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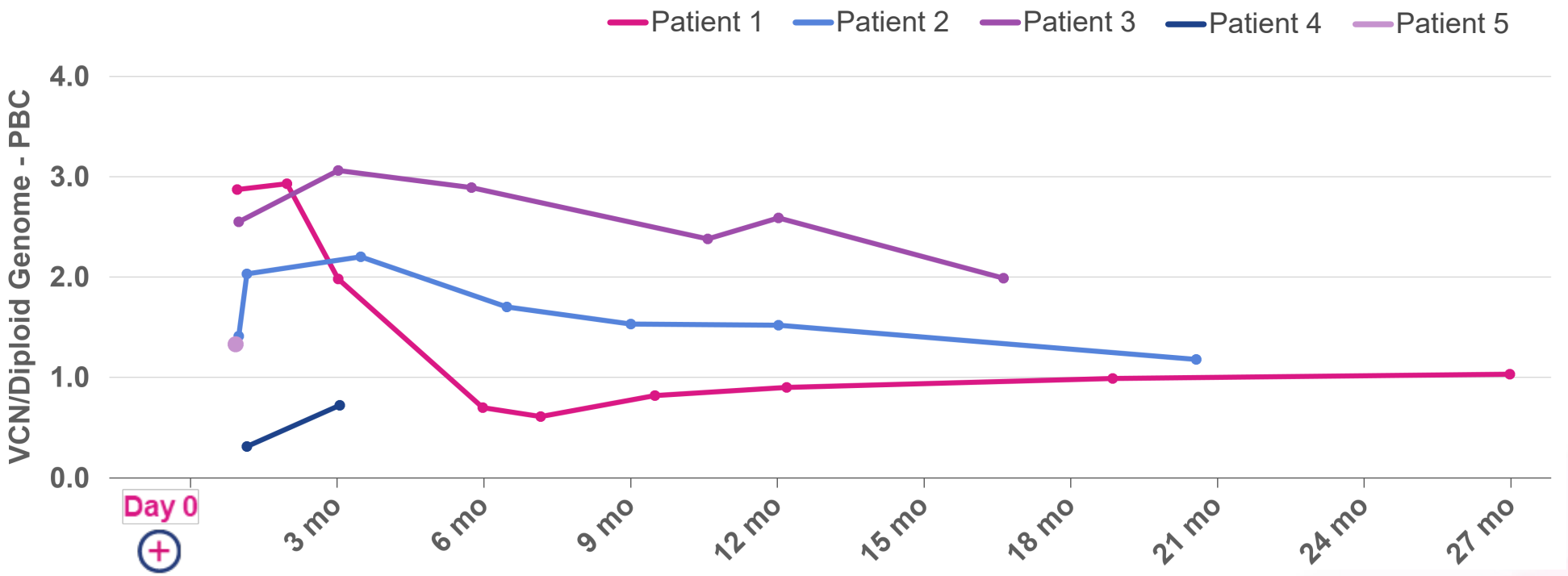
Sustained engraftment to date demonstrated by VCN plateau for patients beyond 12 months

Drug Product VCN/dg	
Patient 1	2.1
Patient 2	1.3*
Patient 3	1.6
Patient 4	0.6
Patient 5	2.5



** From second apheresis; VCN: Vector Copy Number; PBCs: Peripheral Blood Cells; dg: Diploid Genome*

Phase 1/2 Cystinosis trial
(5 patients)

No unexpected safety events or trends related to AVR-RD-04 identified

No SAEs or AEs related to AVR-RD-04 drug product

No SAEs reported

Preliminary AEs reported

- N=40 for subject 1; N=22 for subject 2; N=8 for subject 3; N=25 for subject 4; N=13 for subject 5
- Majority of AEs are mild or moderate
  - 1 severe -- Appendicitis unrelated to study treatment or procedures
- AEs generally consistent with myeloablative conditioning or underlying disease:

Pre-treatment and prior to conditioning (not all events listed)

- Diarrhea, hypokalemia, dizziness
- Dehydration, vomiting

Post-treatment (not all events listed)

- Alopecia, intermittent diarrhea, vomiting, loss of appetite
- Mucositis, intermittent febrile neutropenia, intermittent epistaxis
- Intermittent blurry vision, intermittent hypokalemia, mucoceles
- Thrombocytopenia

AE: Adverse Event; SAE: Serious Adverse Event; safety data cut-off date is May 6, 2022

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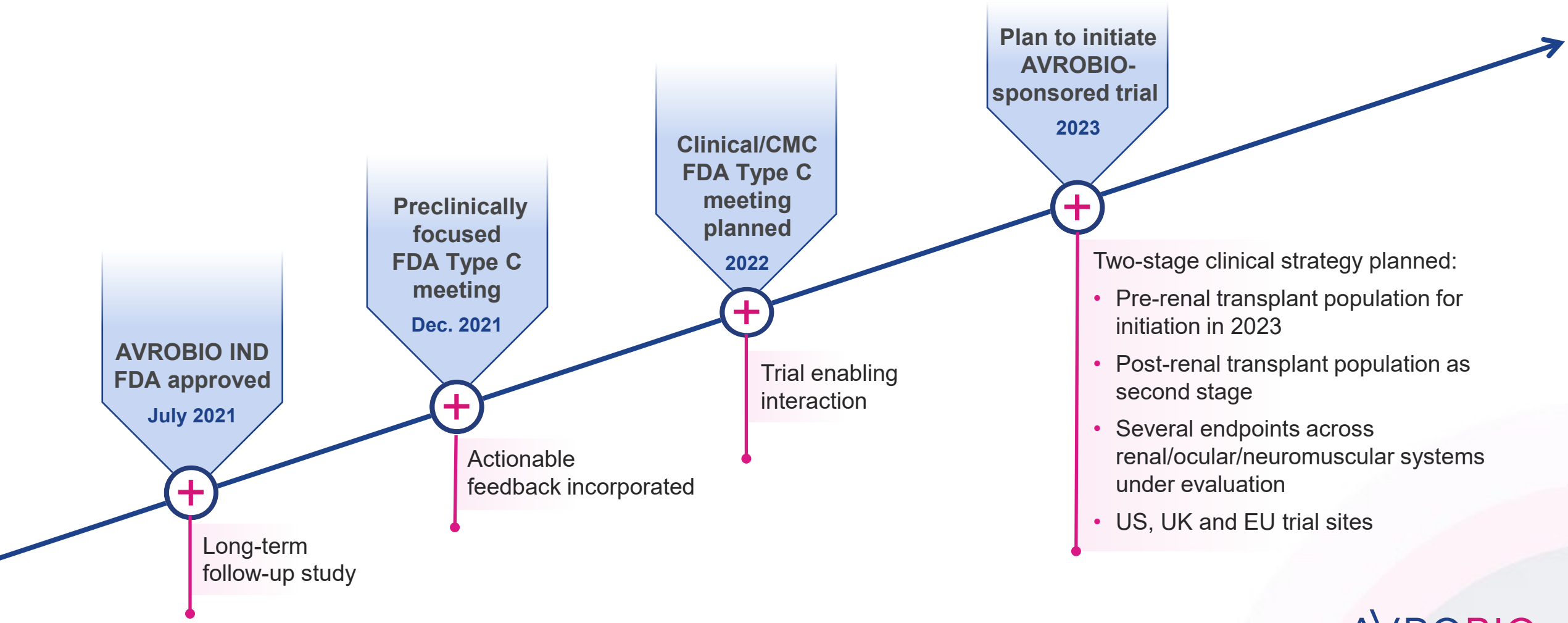
Building regulatory momentum

Active IND with US/EU Orphan Designation and US Fast Track Designation



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Gaucher disease franchise

Gaucher disease type 1 opportunity

Caused by mutation in the gene encoding for glucocerebrosidase (GCase) enzyme

Standard of care (SOC): ERT

- Not curative, relentless progression of disease continues, including bone crisis and fatigue
- Burdensome and expensive – bi-weekly infusions required; 5-year treatment cost with ERT = ~$2.3 million*

Affects ~ 1:44,000 people worldwide

Adrianna, living with Gaucher disease type 1

Unmet needs with SOC:

Everyday burden of illness, and life expectancy
Fatigue, pain, lung disease, biweekly infusions, shortened lifespan

Hemoglobin levels and platelet counts
Anemia, thrombocytopenia, easy bruising, bleeding

Bone-related manifestations
Skeletal abnormalities, avascular necrosis, osteoporosis

CNS complications
Increased risk of GBA-Parkinson's disease

Hepatosplenomegaly
Enlarged liver, enlarged spleen

** WAC pricing from Redbook using standard dosing assumptions*

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Even on ERT, patients endure debilitating symptoms

Incomplete therapeutic response is common:

- **60% failed to achieve** at least one of six therapeutic goals after 4+ yrs of ERT[1]
- Many continue to exhibit **bone pain, organomegaly and cytopenia** after 10 yrs of ERT[2]
- **25% have physical limitations** after 2 yrs of ERT, primarily due to bone disease[3]

Prospective registry of 757 GD1 patients on ERT after 10 years

Persistence after **10 years ERT†**	**Non-splenectomized** Patients	**Splenectomized** Patients
Bone Pain	43%	63%
Splenomegaly*	38%	N/A
Thrombocytopenia*	23%	1%
Hepatomegaly*	14%	19%
Anemia	12%	9%
Bone Crisis	7%	17%

** Higher persistence rates observed when more severe manifestations were present at baseline*
† Persistence refers to the presence of anemia, bone pain, bone crisis, or at least moderate thrombocytopenia, splenomegaly, or hepatomegaly, present after 10 years of ERT among those with baseline involvement of these parameters (from a registry of 757 GD1 patients; Weinreb et al., 2013)
Following 10 years of treatment, ~26% of patients were receiving between 45-150 U/kg EOW, and 96% of these individuals were receiving doses between 45-90 U/kg EOW.
Data rounded to complete integer.
GD1: Gaucher Disease Type 1; ERT: Enzyme Replacement Therapy; EOW: Every Other Week
[1]Weinreb N et al., Amer J Hematol, 2008; [2]Weinreb N et al., J Inherit Metab Dis, 2013; [3]Giraldo P et al., Qual Life Res, 2005

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Guard1: Phase 1/2 study in Gaucher disease type 1

PHASE 1/2

AVR-RD-02

An **open-label, multinational phase 1/2 study of the safety and efficacy** of *ex vivo,* lentiviral vector-mediated gene therapy AVR-RD-02 for patients with Gaucher disease type 1

ACTIVELY RECRUITING:

OBJECTIVES	PATIENTS

• Safety
• Efficacy
• Engraftment
	• Enrollment goal 8-16 patients
	  • 3 patients dosed to date
	• 18-45-year-old males and females
	• Have a confirmed diagnosis of GD1 based on:
	  – Deficient glucocerebrosidase enzyme activity
	  – Clinical features consistent with GD1

Gaucher disease type 1 patients who are:

- ERT-stable for >24 months *or*
- Treatment-naïve *or*
- Have not received ERT or SRT in the last 12 months

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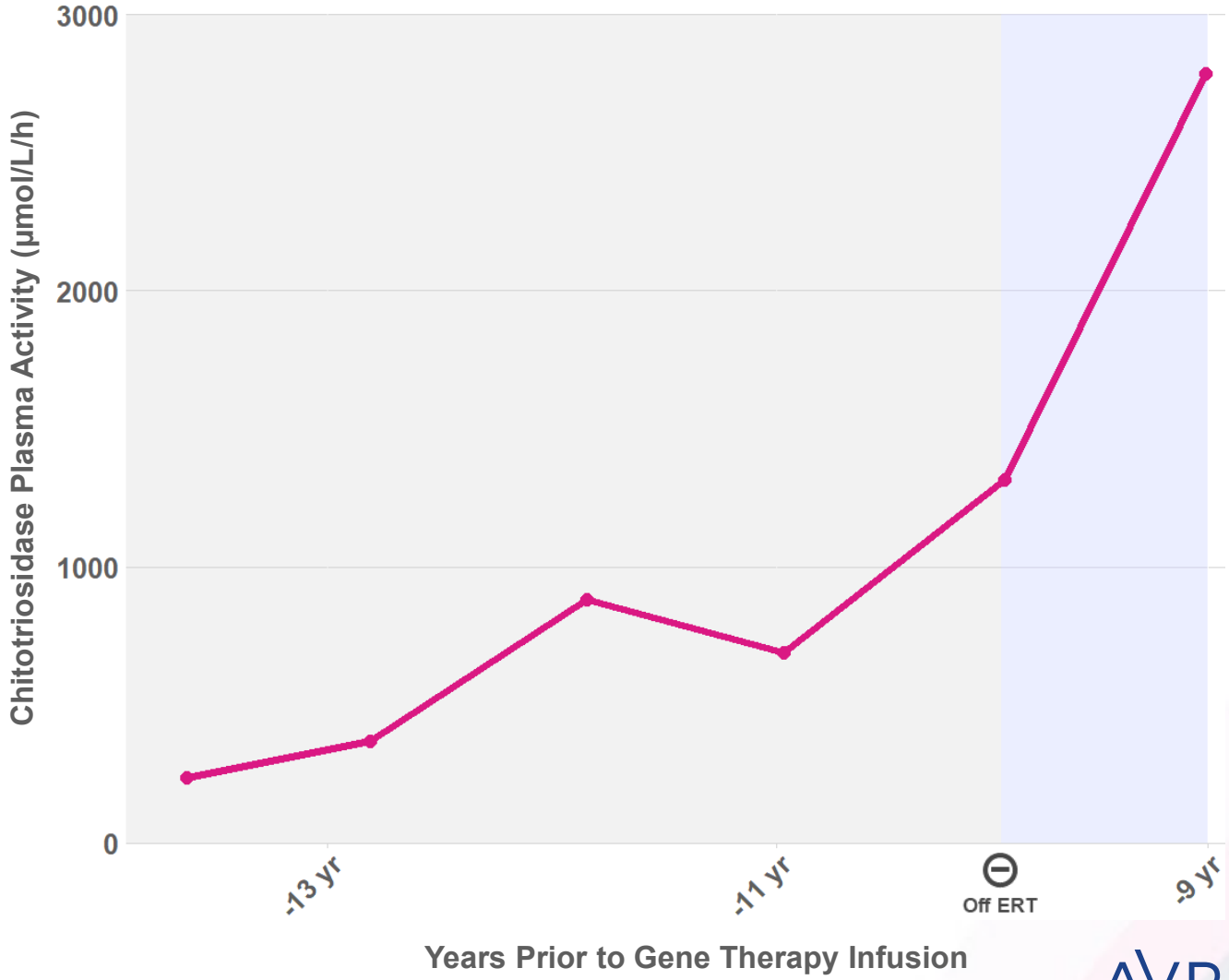
GD1: Gaucher Disease Type 1; ERT: Enzyme Replacement Therapy; SRT: Substrate Reduction Therapy

First patient's plasma chitotriosidase levels spike off ERT

Personal history documents response to intermittent and halted ERT use

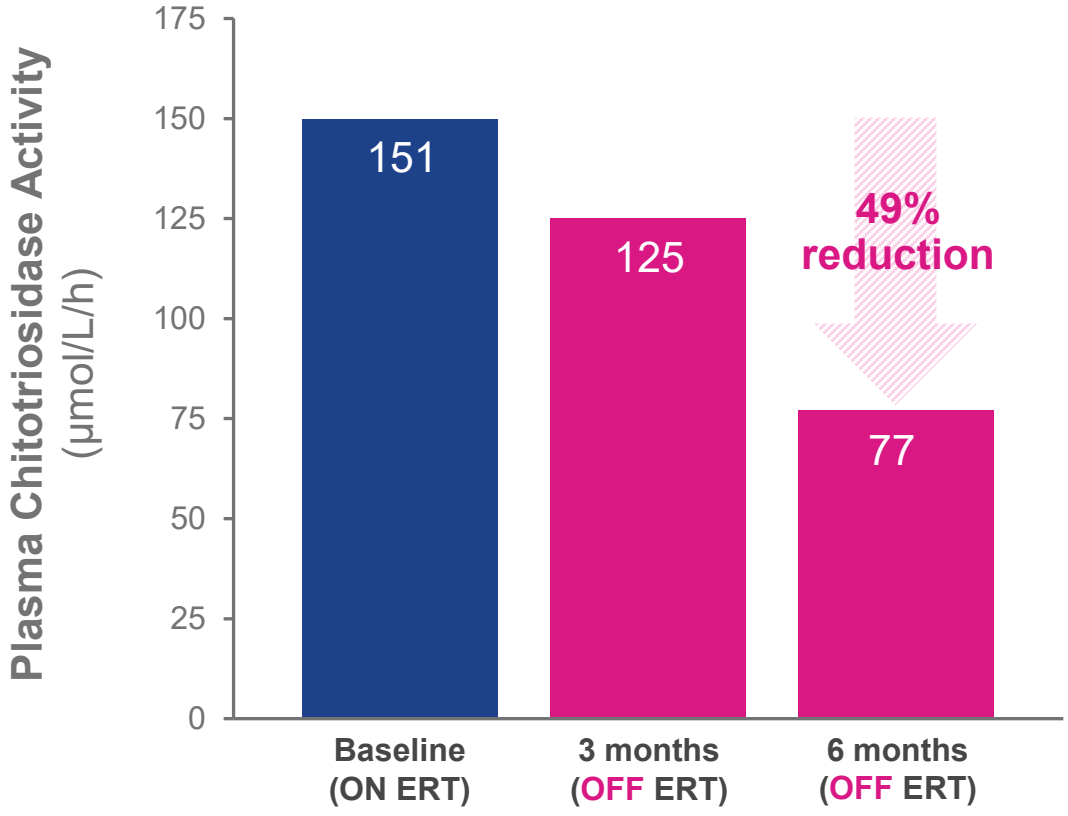
Chitotriosidase is a marker of inappropriately activated macrophages (Gaucher cells)



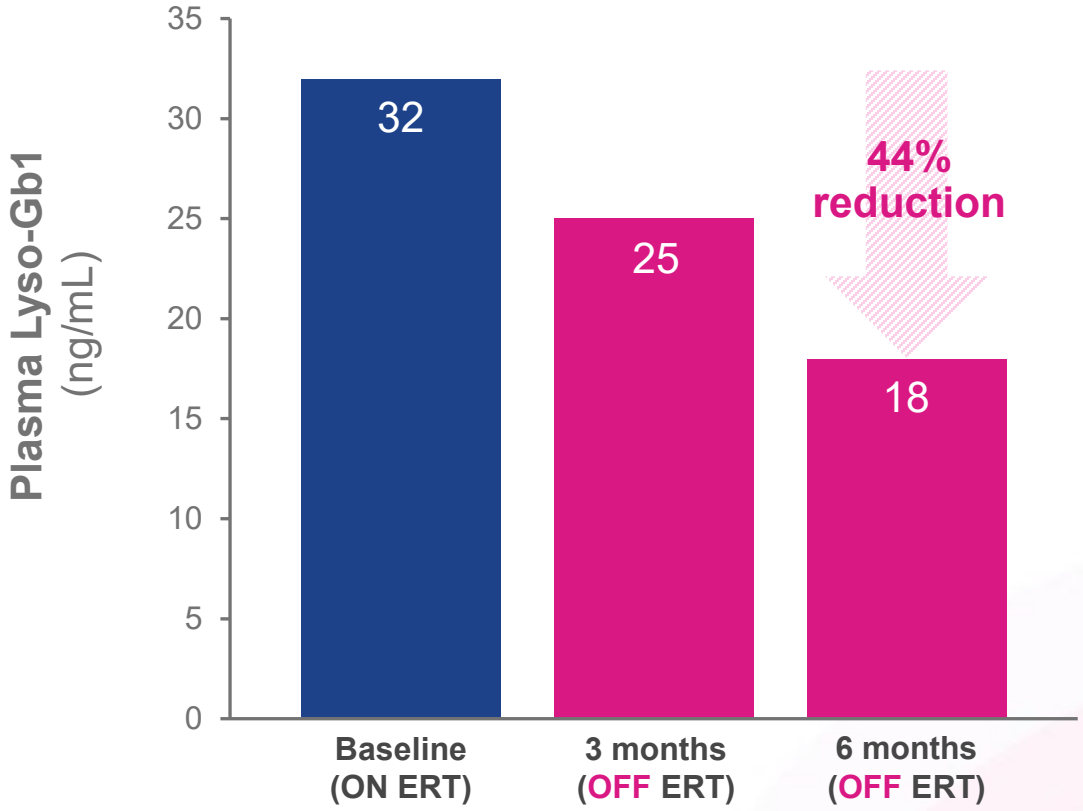
Chitotriosidase Plasma Activity Normal Range: 0.0–44.2 µmoL/L/h
ERT: Enzyme Replacement Therapy

Key biomarkers below ERT baseline at 6 months

Chitotriosidase is a marker of inappropriately activated macrophages (Gaucher cells)



Lyso-Gb1 is a sensitive and specific marker of toxic metabolite accumulation in Gaucher disease



Baseline taken one month prior to gene therapy which is when ERT is discontinued
Lyso-Gb1 Plasma Normal Range: 0.5 – 1.2 ng/mL
Plasma chitotriosidase activity normal range: 0.0 – 44.2 µmoL/L/h
ERT: Enzyme Replacement Therapy

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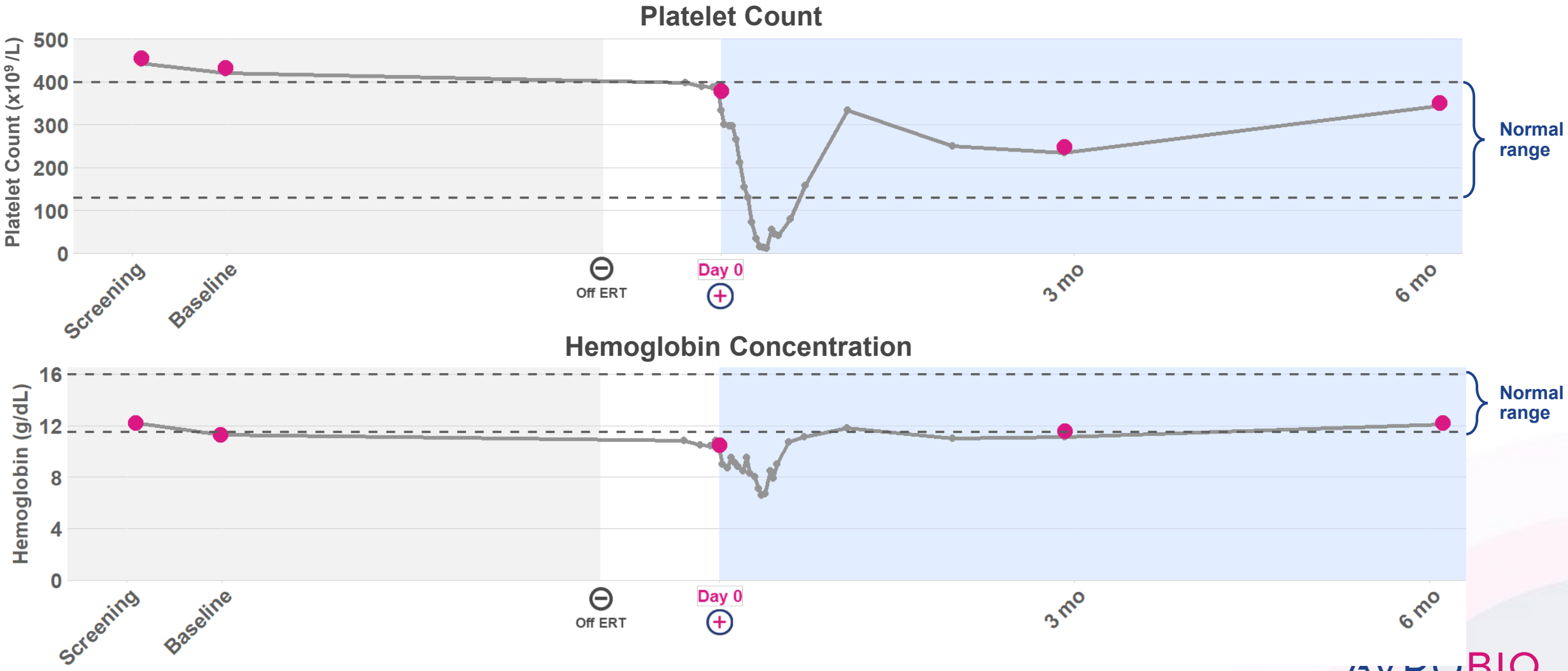
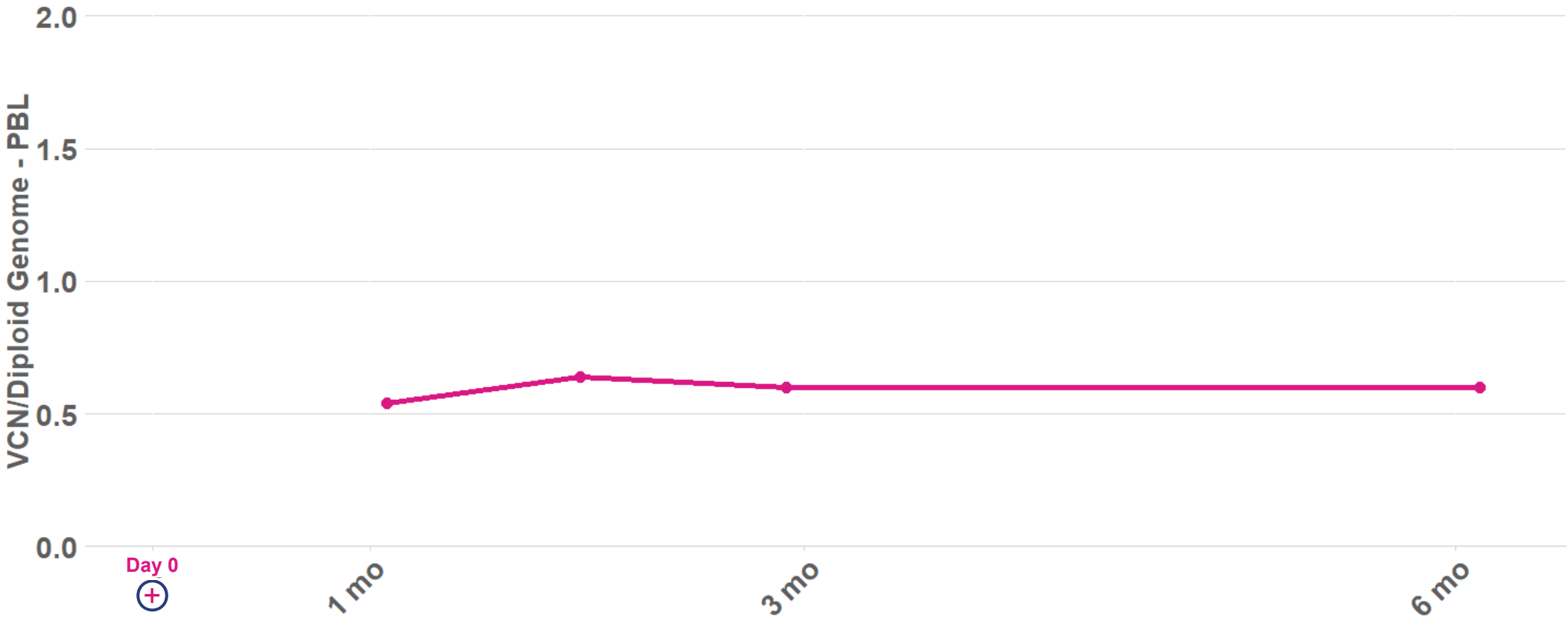
Platelet counts and hemoglobin in normal range at 6 months, despite being off ERT



Platelet Count Reference Value Adult: 130-400x109/L; Hemoglobin Reference Value: Males: 13.5-17.5 g/dL; Females: 11.5-16.0 g/dL; grey line: local (safety) lab values; pink dots: central (efficacy) lab values; ERT: Enzyme Replacement Therapy

VCN trending as expected at 6 months

Drug Product VCN/dg	
Patient 1	3.7



VCN, vector copy number; PBL, peripheral blood leukocytes; dg, diploid genome

No unexpected safety events 12+ months post dosing

No SAEs or AEs related to drug product

AEs are consistent with myeloablative conditioning, drugs mandated by protocol or study procedures, underlying disease and pre-existing conditions

No SAEs reported

AEs reported, n= 37

Event severity assessment

- 26 AEs were Grade 1 or Grade 2
- 11 AEs were Grade 3 or 4
  - Anemia, leukopenia, neutropenia, thrombocytopenia, eye pain, decreased appetite, dehydration, headache, hypophosphatemia, amenorrhea*

Event causality assessment

- 21 AEs definitely, probably or possibly related to busulfan (N= 1 patient dosed)
- 8 AEs definitely, probably or possibly related to G-CSF** (N= 2 patients enrolled)
- 1 AE definitely, probably or possibly related to Plerixafor (N= 2 patients enrolled)

AVR-RD-02 has not been approved by the FDA or by any other regulatory body and its safety and efficacy has not been established
Note: Safety database cut as of August 31, 2021
AE, adverse event; SAE, serious adverse event; G-CSF, granulocyte colony stimulating factor
** Unresolved and ongoing as of the safety database cut of August 31, 2021*
***Two of the AEs, dehydration and decreased appetite, are noted as related to both G-CSF and busulfan administrations*

Gaucher disease type 3 opportunity

Subacute neurological form of Gaucher disease characterized by progressive encephalopathy and associated with the systemic manifestations of Gaucher type 1

Standard of care (SOC): ERT

- Not curative, relentless progression of disease continues; utility of ERT minimized by its inability to impact the CNS
- Burdensome and expensive – bi-weekly infusions required; 5-year treatment cost with ERT = ~$2.3 million*

Unmet needs with SOC:

Bone-related manifestations
Bone crises, bone pain, avascular necrosis

CNS complications
Seizures, cognitive problems, poor coordination

Everyday burden of illness and life expectancy
Fatigue, pain, shortened lifespan

Hemoglobin levels and platelet counts
Anemia, thrombocytopenia, easy bruising, bleeding

Hepatosplenomegaly
Enlarged liver, enlarged spleen

Maddie, living with Gaucher disease Type 3

** WAC pricing from Redbook using standard dosing assumptions*

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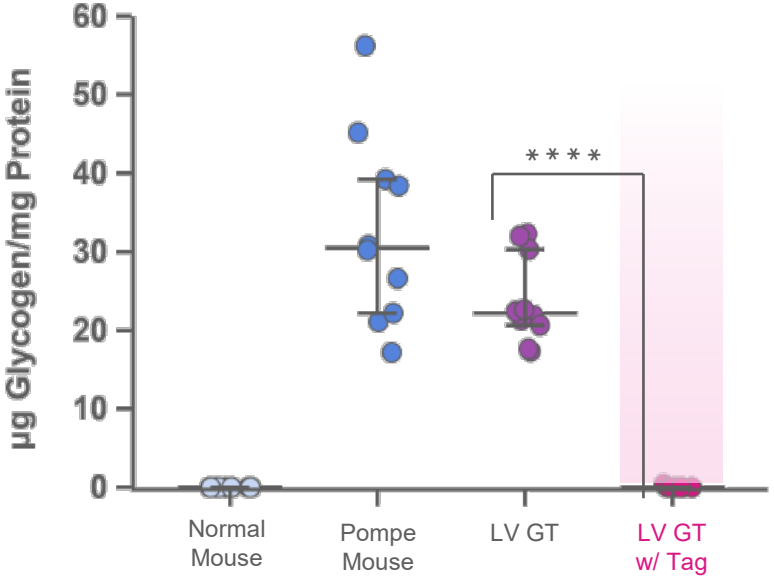
Second wave programs

Advancing Pompe and Hunter programs to the clinic

Regulatory meetings planned for 2H 2022

Pompe disease

GT + Tag normalizes glycogen substrate in brain

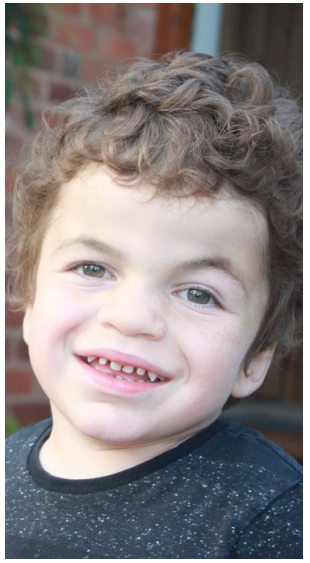


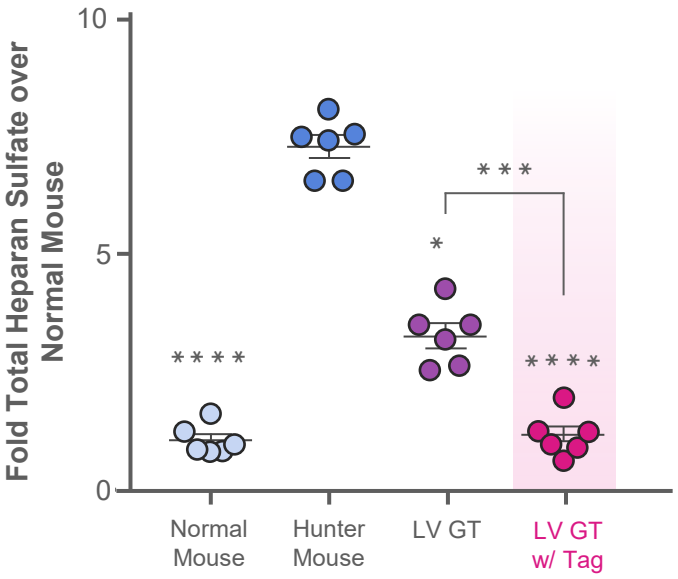
Unmet needs with SOC:

- Pulmonary function
- CNS complications
- Physical endurance and strength
- GI complications

Hunter syndrome

GT + Tag normalizes heparan sulfate in brain





Unmet needs with SOC:

- Neurological complications
- Respiratory and cardiac system
- Skeletal and connective tissue
- Burden of illness and life expectancy

*Figure adapted from Gleitz H et al., EMBO Mol Med, 2018 Fig 3A; *P<0.05, ***P<0.001, ****P<0.0001; LV GT: Lentiviral Gene Therapy*

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Near-term opportunities in leading gene therapy pipeline

Potential billion-dollar revenue opportunities

AVR-RD-04 for cystinosis

- First and only gene therapy for cystinosis in clinic
- Proof-of-concept demonstrated in adults
- Secured U.S./EU Orphan Disease Designation and U.S. Fast Track Designation

- Plan to meet with regulators in 2H 2022 to discuss company-sponsored trial
- Plan to initiate company-sponsored trial in 2023

AVR-RD-02* for Gaucher disease type 3

- Second program in Gaucher disease franchise
- Leverages clinical and CMC work conducted in Gaucher disease type 1, which was first gene therapy for Gaucher to enter clinical trials

- Plan to engage with regulators on potential Phase 2/3 trial in 2H 2022
- Plan to initiate potential Phase 2/3 trial in 2023

Other anticipated 2022 catalysts:

- AVR-RD-02 for Gaucher disease type 1 – planned clinical update
- AVR-RD-05 for Hunter syndrome – CTA authorization expected
- AVR-RD-03 for Pompe disease – engage with regulators on clinical trial

*Planned regulatory milestones subject to regulatory agency clearance; * Formerly referred to as AVR-RD-06; collaborator-sponsored Phase 1/2 clinical trial of AVR-RD-04 is funded in part by grants to UCSD from the California Institute for Regenerative Medicine (CIRM), Cystinosis Research Foundation (CRF) and National Institutes of Health (NIH)*

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Thank you

Appendix

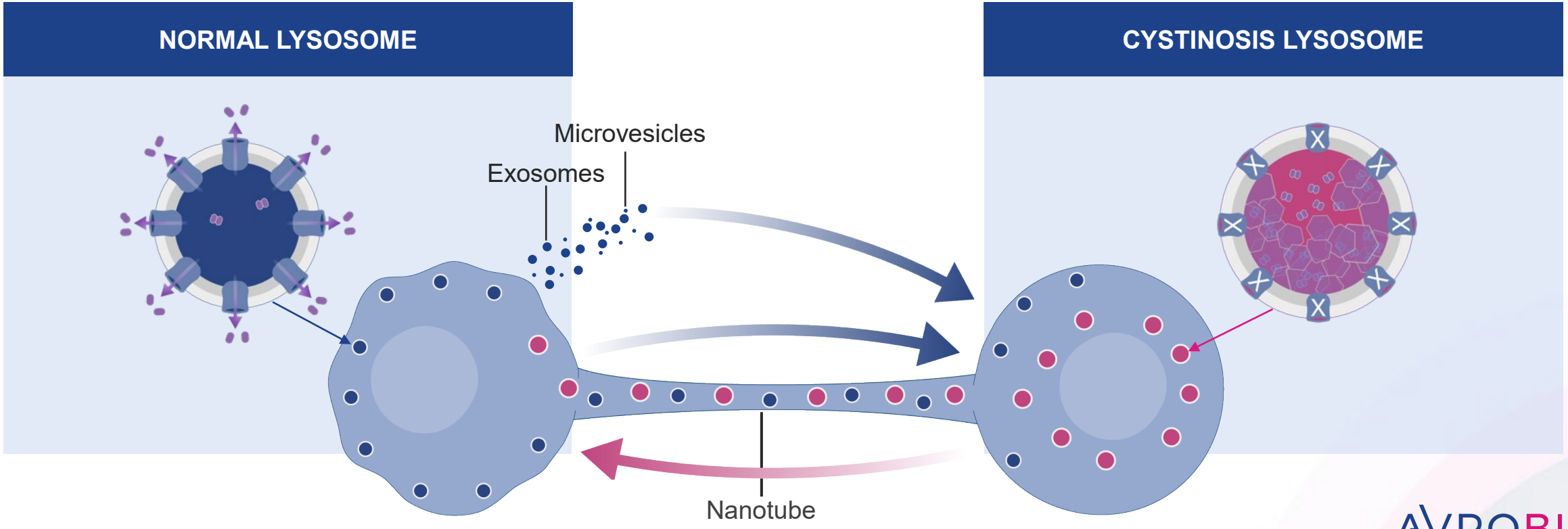
Genetically modified macrophages restore normal cystine recycling in mouse model

Mechanisms of action

Macrophages with CTNS transgene restore cystine recycling to CTNS^{-ve} cells via:

1. Exosomes / Microvesicles – transfer of cystinosin, CTNS mRNA
2. Tunneling nanotubes – transfer of corrected lysosomes, cystinosin, CTNS mRNA

Net result: Corrected lysosomes in cells



Sources: Naphade, Stem Cells, 2015. Harrison, Molecular Therapy, 2013.
CTNS: cystinosin, lysosomal cystine transporter; mRNA: Messenger Ribonucleic Acid

Cystinosis is an attractive commercial market

SOC is burdensome

- Shortcomings of cysteamine pills often lead to poor patient compliance:
  - Cause sulfur odor on body and breath
  - High daily pill burden can lead to GI discomfort and vomiting

SOC does not stop disease progression

Disease symptoms persist despite SOC:

Kidney function
Frequently require multiple kidney transplants

Vision
Corneal cystine accumulation, photophobia

CNS and muscular complications
Myopathy, hypotonia, neurodevelopmental issues

Endocrine disorders
Softening & deformation of bones, hypothyroidism, diabetes, infertility

Billion-dollar revenue opportunity

- 5-year cystinosis SOC treatment cost ~$4.3 million* in U.S.
- ~1,600 patients in U.S., Europe and Japan alone
- Most severe form, infantile nephropathic cystinosis, affects ~95% of cystinosis population

** SOC: standard of care; WAC pricing from Redbook using standard dosing assumptions. Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate), midpoint between avg. adult and pediatric*

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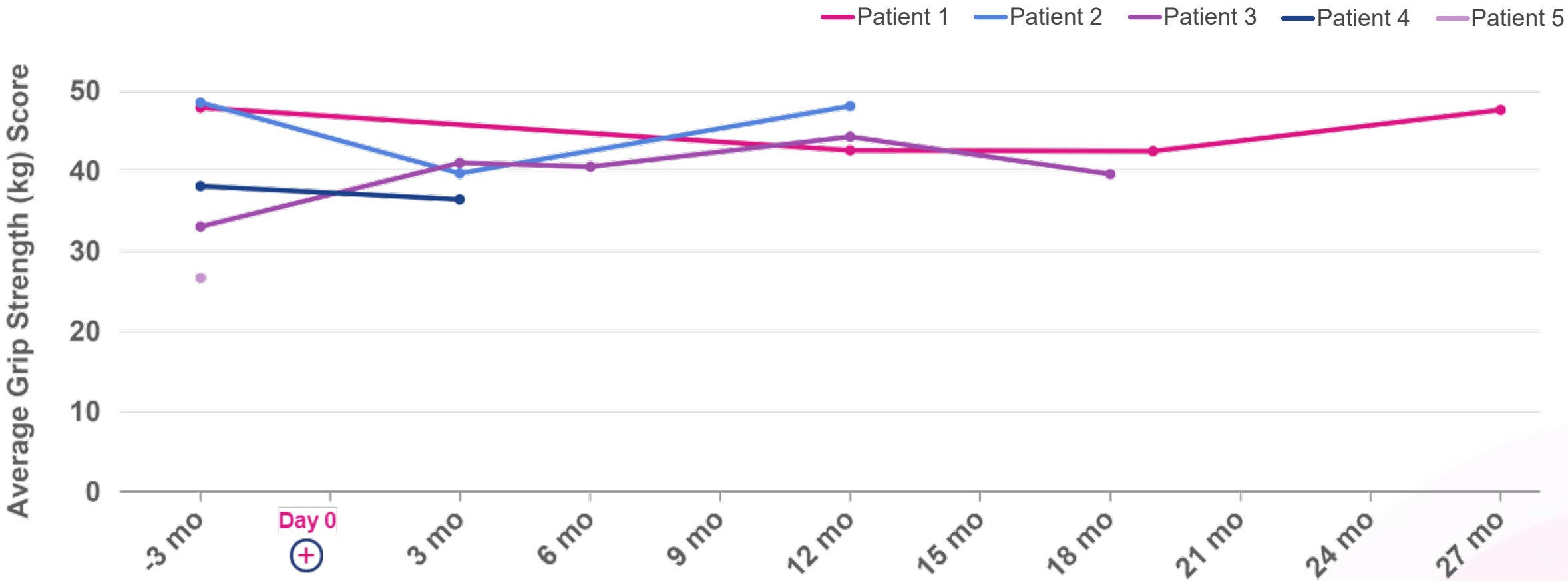
Average grip strength stable up to 27 months

Disease progression typically leads to loss of muscle strength over time



Average Grip Strength (kg) is defined as the average of the largest reading from each hand

Patient baseline characteristics

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4	PATIENT 5
Age of symptom onset/diagnosis	0 year / 8 months	0 year / 6 months	4 years	6 years	8 months
Age dosed with CTNS-RD-04	20 years Infused October 2019	46 years Infused June 2020	22 years Infused November 2020	33 years Infused November 2021	31 years Infused March 2022
Gender	Male	Male	Male	Male	Female
Mutation	• 57-kb deletion • c.696dupC, p.Val233Argfs*63	• 57-kb deletion • c.473T>C, p.Leu158Pro	• c.18_21del, p.Thr7Phefs*7 • c.295_298del, p.Val99Ilefs*18	• 57-kb deletion • c.473T>C, p.Leu158Pro	• 57-kb deletion • c.414G>A, p.Trp138*
Kidney transplant status and cysteamine dosing prior to CTNS-RD-04 dosing	• No kidney transplant; stage 3 (moderate CKD) renal failure • On oral Cysteamine • On Cysteamine drops	• 2 renal transplants (1987 and 1999) • On oral Cysteamine • On Cysteamine drops	• 1 renal transplant (2010) • On oral Cysteamine • On Cysteamine drops	• 2 renal transplants (2008 and 2017) • On oral Cysteamine • Off Cysteamine drops	• No renal transplant; stage 3 (moderate CKD) renal failure • On oral Cysteamine • On Cysteamine drops
Manufactured CTNS-RD-04 product and busulfan dose	• 7.88 x 10e6 CD34+ cells/kg • VCN: 2.07 • 94% viability • AUC Bu: 81.8 mg.h/L	• 5.07 x 10e6 CD34+ cells/kg • VCN: 1.27 • 91% viability • AUC Bu: 86.7 mg.h/L	• 9.59 x 10e6 CD34+ cells/kg • VCN: 1.59 • 95% viability • AUC Bu: 90 mg.h/L	• 3.63 x 10e6 CD34+ cells/kg • VCN: 0.59 • 90% viability • AUC Bu: 88.5 mg.h/L	• 9.12 x 10e6 CD34+ cells/kg • VCN: 2.5 • 95% viability • AUC Bu: 88.2 mg.h/L

Early cystinosis treatment is essential to prevent kidney complications

Disease phenotype	Nephropathic cystinosis	
	Infantile	Juvenile ("late-onset")
Frequency[1]	~95% of patients	<5% of patients
Characteristics of phenotype[1]	• Clinical symptoms related to renal Fanconi syndrome during **first year of life** – **Fanconi syndrome:** Defect of kidney tubules resulting in malabsorption of electrolytes / substances in kidneys[2] • Frequently require **multiple renal transplants with lifetime of immunosuppression** • **Most severe form** of cystinosis	• Usually diagnosed **later in childhood or during adolescence** (after age 10) • Typically experience **renal Fanconi syndrome and proteinuria** • Frequently require **multiple renal transplants with lifetime of immunosuppression**

Source: Simon-Kucher & Partners 2020. 1. Emma et al. (2014). Nephropathic Cystinosis: an international consensus document. Nephrology Dialysis Transplantation, 29(4), iv87-iv94; 2. Keefe et al. (2020). Fanconi Syndrome. StatPearls.

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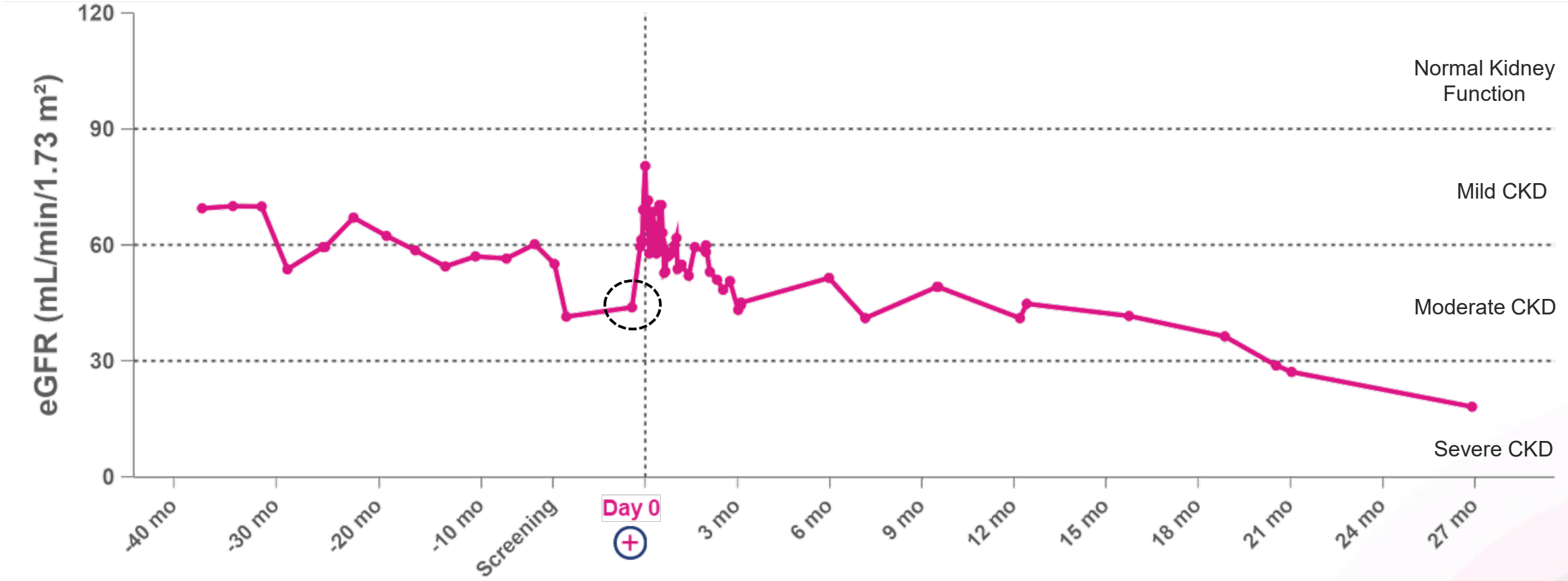
eGFR data reinforce need for early intervention

Entered trial with progressive kidney disease (eGFR of 48), decline accelerates in line with natural history



eGFR: Estimated Glomerular Filtration Rate; eGFR calculated using CKD-EPI formula

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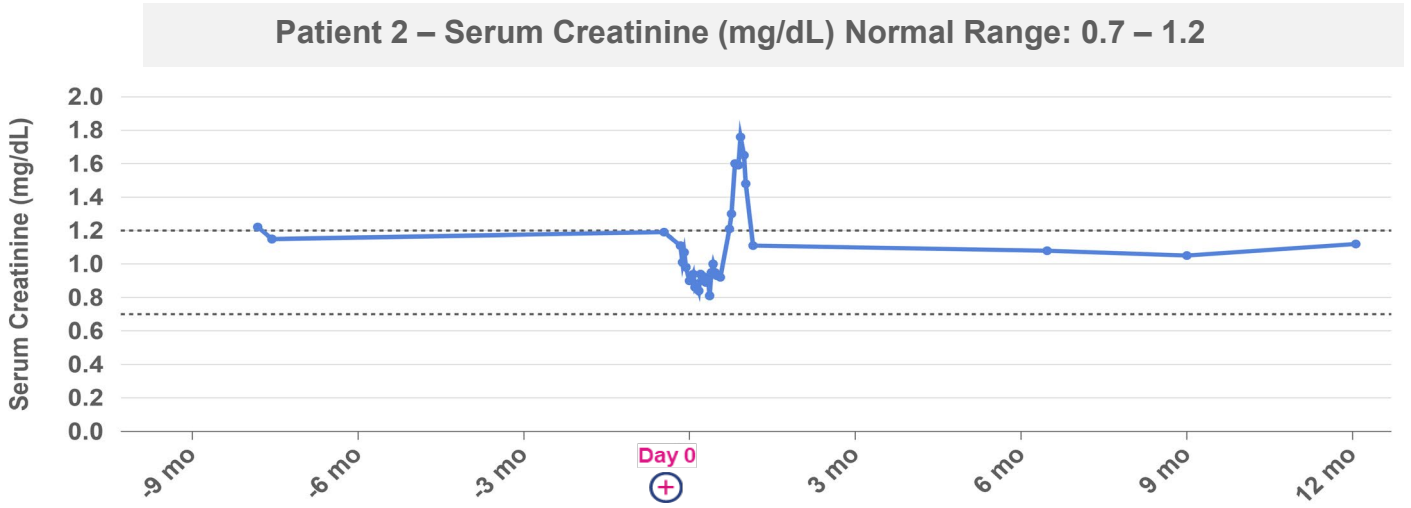
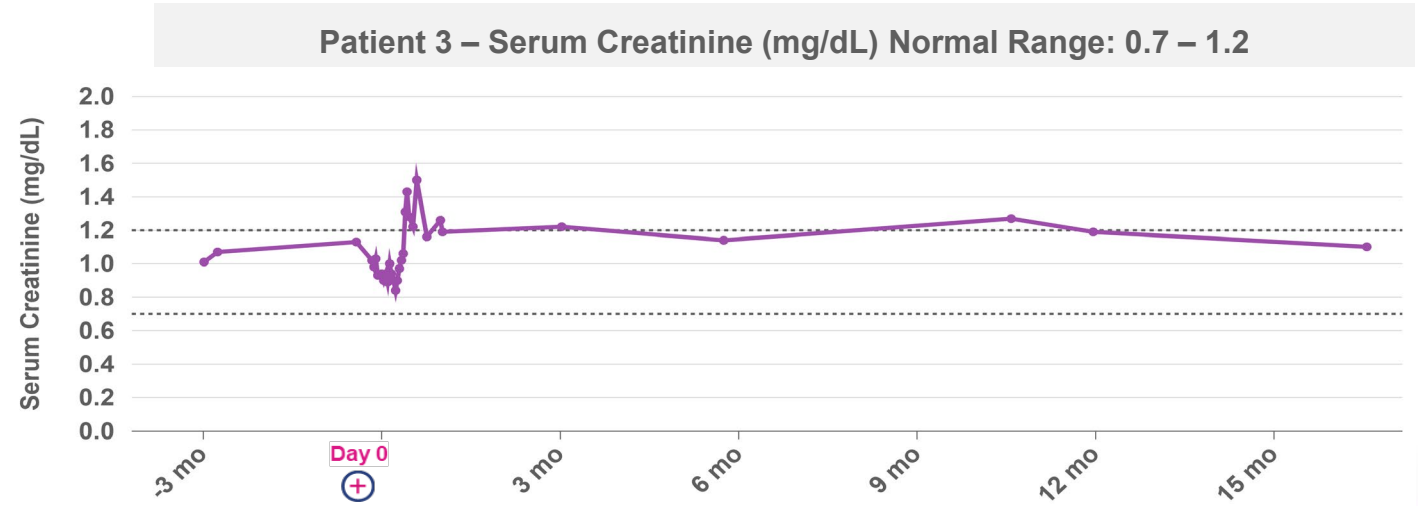
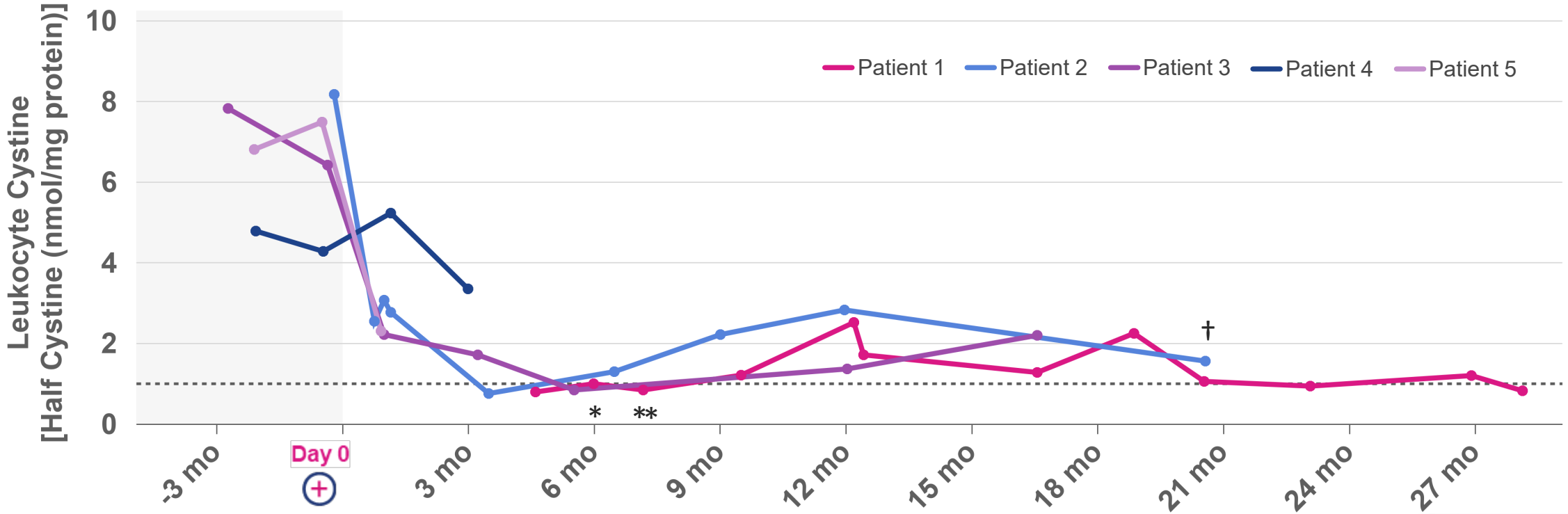
Transplanted kidney not impacted by treatment, as expected

Serum creatinine remains stable post infusion





Leukocyte cystine levels in blood suppressed out to 28 months



*Note: Data from Patient 1 up to 12 months have been previously disclosed. Therapeutic range is <1.0 Half Cystine (nmol/mg protein). Measure of 1 is level of healthy heterozygote.; For Patient 1, Leukocyte Cystine Quantification was initiated at approximately week 20 ; *Patient 1: Hemolyzed sample which may potentially lead to lower results; **Patient 1: Sample processed outside of the range of the stability; †Patient 2: Sample was not collected and shipped according to study protocol*

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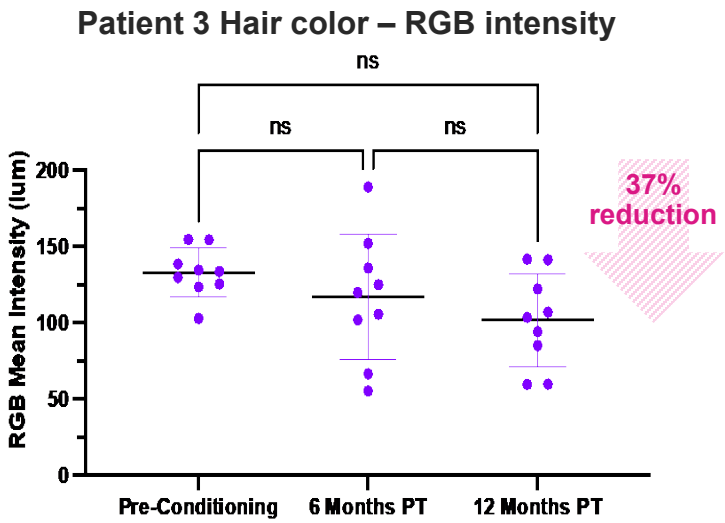
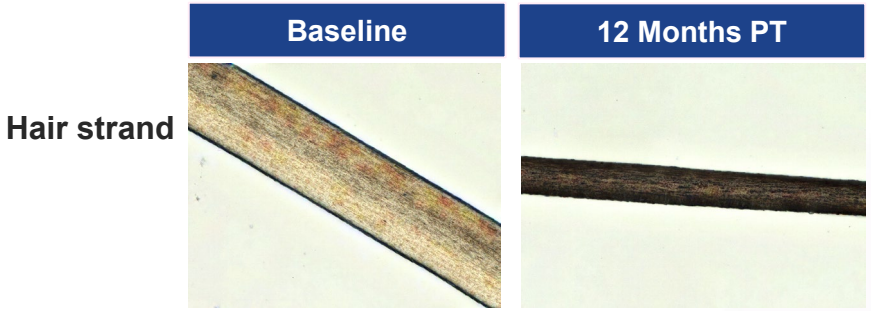
Darker pigmentation may be a sign of multi-functional cystinosin activity post gene therapy

Further enforces systemic reach of gene therapy

Cystinosin is located in melanosomes and regulates melanin synthesis

PATIENT 3*





Source: Do not have permission to show patient image; Chiaverini et al., FESEB, 2012*