UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 17, 2022

AVROBIO, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-38537	81-0710585
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

One Kendall Square
Building 300, Suite 201
Cambridge, MA 02139
(Address of principal executive offices, including zip code)

(617) 914-8420
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**AVRO**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On May 17, 2022, AVROBIO, Inc. (the "Company") issued a press release titled "AVROBIO Reports Positive Data from Phase 1/2 Clinical Trial of Investigational Gene Therapy for Cystinosis, including New Interim Data on Neurocognitive Measures." A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

On May 17, 2022, the Company updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the slide presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, shall not be deemed "filed" for purposes of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	AVROBIO, Inc. press release, dated May 17, 2022.
99.2	AVROBIO, Inc. slide presentation, dated May 17, 2022.
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBR

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AVROBIO, INC.

Date: May 17, 2022

By: /s/ Geoff MacKay
Geoff MacKay
President and Chief Executive Officer

AVROBIO Reports Positive Data from Phase 1/2 Clinical Trial of Investigational Gene Therapy for Cystinosis, including New Interim Data on Neurocognitive Measures

New early data show key visual motor integration, visual perception and motor coordination measures impacted by cystinosis stabilized or improved post gene therapy

Systemic reach of AVR-RD-04 observed across multiple other measures

All five dosed patients remain off oral cysteamine post gene therapy

Continued favorable safety profile with no adverse events related to drug product to date

Clinical proof-of-concept in adult patients lays groundwork for AVROBIO-sponsored clinical trial planned to begin in 2023

CAMBRIDGE, Mass.—(BUSINESS WIRE)—May 17, 2022—AVROBIO, Inc. (Nasdaq: AVRO), a leading clinical-stage gene therapy company with a shared purpose to free people from a lifetime of genetic disease, today reported new interim data, including on new visual motor integration, motor coordination and visual perception measures, from a collaborator-sponsored, ongoing Phase 1/2 gene therapy clinical trial[i] of AVR-RD-04, an investigational gene therapy for cystinosis, at the 25th Annual Meeting of American Society for Gene and Cell Therapy (ASGCT) in Washington D.C., May 16-19, 2022.

The collaborator-sponsored Phase 1/2 clinical trial is evaluating the safety and efficacy of AVR-RD-04 in adult patients diagnosed with the infantile form of cystinosis who previously had been treated with the current standard of care (SOC) cysteamine. AVR-RD-04 genetically modifies patients' own hematopoietic stem cells (HSC) to express a functional version of cystinosin, the protein that is deficient in people living with cystinosis. Preliminary data suggest that post gene therapy, functional cystinosin has been produced throughout the body as evidenced by clinical measures in multiple tissues, including the eyes, skin, gastrointestinal mucosa and neurocognitive system. No adverse events (AEs) related to the drug product have been reported to date.

"We're thrilled with our progress in this first and only gene therapy trial for cystinosis, a devastating genetic disease with unmet medical needs that impact the daily lives of patients and their families," said Stephanie Cherqui, Ph.D., lead investigator of the clinical trial and associate professor of Pediatrics at the University of California San Diego (UCSD). "Now with data from up to five patients, we have observed a strong safety and tolerability profile, as well as a reduction in the harmful accumulation of cystine crystals in cells across multiple tissues.

"All five patients dosed to date remain off oral cysteamine. We believe the results to date for this investigational gene therapy show its potential to stabilize or reduce impact of cystinosis on different tissues with a single dose," she added.

[i] 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).

The 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).

“We believe the interim data from this ongoing clinical trial demonstrate the potential of gene therapy using patient’s own hematopoietic stem cells to impact the body head-to-toe by restoring functional cystinosin and reducing the accumulation of cystine crystals systemically,” said AVROBIO Chief Medical Officer, Essra Ridha, M.D., MRCP, FFPM. “Cystinosis is a devastating disease that currently carries a 5-year treatment cost in excess of $4 million per patient in the U.S. and impacts approximately 1,600 patients in the U.S., Europe and Japan alone. With proof-of-concept demonstrated, we continue to lay the groundwork for an AVROBIO-sponsored clinical trial planned to begin in 2023 and look forward to our interactions with regulators on our clinical and Chemistry Manufacturing and Controls (CMC) strategy later this year.”

Key motor coordination and visual perception measures stabilize or show positive trends post gene therapy

Visual motor integration (VMI) measured with the Beery – Buktenica Developmental Test of VMI, a standardized test evaluating the ability of the brain to interpret and translate visual information into an exact motor response, has been shown to be a consistent indicator of visual spatial and visual motor dysfunction in patients with cystinosis. These measures do not generally improve over time in this population.

Early data indicate that post gene therapy the two patients with data to date show stabilization of scores on the Beery – Buktenica Developmental Test of VMI and importantly, improvement in the subtests of motor coordination and visual perception, suggesting a potential impact on the neuropathology of the disease. In patient #1, an approximate 20-point improvement was evident in both visual perception and motor coordination, and in patient #3 a 5-point increase in visual perception was detected, with motor coordination rising by 45 points in the first 6 months post treatment and a more modest rise thereafter.

In addition, following discontinuation of cysteamine, average hand grip strength remained stable up to 27 months after dosing.

Systemic reach of AVR-RD-04 also seen across measurements of blood, eye, skin and gastrointestinal mucosa

Early data indicate that post gene therapy, patients have been able to produce and distribute functional cystinosin protein throughout the body, which prevents the pathological accumulation of cystine crystals. In blood, the leukocyte cystine levels decreased measurably, with the three patients out more than 12 months post gene therapy stabilizing near 1.0 nmol/mg protein.

Photophobia, or extreme visual sensitivity to light, is a hallmark of cystinosis. In a patient-reported outcome scale of photophobia severity, the first three patients for which data are available, reported improved or stable photophobia scores. Patient #1, who entered the trial with a higher level of cystine crystal accumulation in the eye, reported a two-point photophobia score improvement 24 months post gene therapy. Patients #2 and #3, who both entered the trial with relatively lower cystine crystal accumulation in the eye, reported stable photophobia scores, both at 12 months post gene therapy. Patients #1, #3, #4 and #5 remain off cysteamine eye drops.

A decline in cystine crystals was observed in skin and gastrointestinal mucosa biopsies from the first three patients. Patients with cystinosis accumulate cystine crystals in cells, which leads to tissue and organ damage and results in debilitating co-morbidities. In the skin, reductions in average intracytoplasmic crystals per cell ranged from 8% in patient #1, 64% in patient #2 and 81% in patient #3 below the patients' own standard-of-care baseline measures at 12-27 months post gene therapy. In the intestinal mucosa, a measurable reduction below patients' own standard-of-care baseline measures was observed post gene therapy, including for patient #1 a 73% reduction after 27 months, for patient #2 a 28% reduction after 12 months and for patient #3 an 83% reduction after 18 months. These data suggest the systemic distribution of functional cystinosis protein is impacting a variety of measures throughout the body. Biopsies have not yet been conducted for patient #4 and #5, who have been more recently infused.

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

Patients with cystinosis frequently exhibit blond or lighter-colored hair and fair complexion because of reduced levels of melanin in their skin. *In vitro* studies have demonstrated that cystinosin is located in melanosomes of melanocytes and when functional cystinosin is absent or reduced, melanin pigment synthesis is inhibited.

New early quantitative data suggest that gene therapy-derived cystinosin may restore melanin production. Twelve months after infusion, two patients exhibited progressively darkening hair color, as measured by a 25% and 37% reduction in red, green, blue (RGB) mean intensity for patient #1 and patient #3, respectively, further indicating cystinosin protein throughout the body. In this case, a microscope was used to obtain high resolution images of hair strands. The images were taken using transmitted light at 20x magnification and analyzed for RGB intensity with numerical values assigned to quantify the level of pigmentation. These data are not yet available for patients #2, #4 and #5.

Sustained engraftment demonstrated with stable VCN for patients beyond 12 months

Importantly, sustained engraftment has been observed in the first three patients, as evidenced by stable vector copy number (VCN) levels. At 17- to 27-months post gene therapy, their VCN is between 1.0 and 2.0 per diploid genome. The recently dosed fourth and fifth patient have a VCN of 0.7 and 1.3 per diploid genome at three-months and one-month post gene therapy, respectively.

Safety and tolerability profile remains strong

Safety data from the five patients dosed to date indicate no AEs related to drug product. All AEs were related to myeloablative conditioning, stem cell mobilization, underlying disease or pre-existing conditions. The majority of AEs were mild or moderate and resolved without clinical sequelae.

Further details on the collaborator-sponsored Phase 1/2 trial (NCT03897361) are available on clinicaltrials.gov. For more information on the cystinosis trial data presented at ASGCT, please see data slides here.

AVROBIO-sponsored trial on track for 2023

Based on the data reported today, combined with feedback provided by the U.S. Food and Drug Administration (FDA) after a fall 2021 Type C meeting, and pending the outcome of further planned regulatory authority interactions this year, the company expects to initiate an AVROBIO-sponsored trial in 2023 in the U.S., followed by sites in the UK and Europe. AVROBIO's current plan involves a two-part strategy, beginning in a pre-renal transplant population followed by a post-renal transplant population.

About cystinosis

Cystinosis is a rare, progressive disease marked by the accumulation of cystine in cellular organelles known as lysosomes. This buildup causes progressive organ damage and debilitating corneal damage, swallowing dysfunction, chronic kidney disease leading to end-stage renal disease and muscle wasting leading to a shortened lifespan. Currently, more than 90% of treated cystinosis patients require a renal transplant in the second or third decade of life. The current standard of care for cystinosis is cysteamine, a treatment regimen that can require dozens of pills per day, does not prevent overall disease progression and carries side effects, such as breath and body odor and gastrointestinal complications, which may be difficult to tolerate.

About AVROBIO

Our vision is to bring personalized gene therapy to the world. We aim to prevent, halt or reverse disease throughout the body with a single dose of gene therapy designed to drive durable expression of therapeutic protein, even in hard-to-reach tissues and organs including brain, muscle and bone. AVROBIO's pipeline is powered by our industry-leading plato® gene therapy platform, our foundation designed to deliver gene therapy worldwide. It includes clinical programs in cystinosis and Gaucher disease type 1, as well as preclinical programs in Gaucher disease type 3, Hunter syndrome and Pompe disease. We are headquartered in Cambridge, Mass. For additional information, visit avrobio.com, and follow us on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words and phrases such as "aims," "anticipates," "believes," "could," "designed to," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words and phrases or similar expressions that are intended to identify

forward-looking statements. These forward-looking statements include, without limitation, statements regarding our business strategy for and the potential therapeutic benefits of our product candidates, including AVR-RD-04 for the treatment of cystinosis, the design, commencement, enrollment and timing of ongoing or planned clinical trials, clinical trial results, product approvals and regulatory pathways, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, timing and likelihood of success, the expected benefits and results of our implementation of the plato platform in our clinical trials and gene therapy programs, and the expected safety profile of our investigational gene therapies. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Results in preclinical or early-stage clinical trials may not be indicative of results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

Any forward-looking statements in this press release are based on AVROBIO's current expectations, estimates and projections about our industry as well as management's current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of AVROBIO's product candidates, including AVR-RD-04 for the treatment of cystinosis, will not be successfully developed or commercialized, the risk of cessation or delay of any ongoing or planned clinical trials of AVROBIO or our collaborators, the risk that AVROBIO may not successfully recruit or enroll a sufficient number of patients for our clinical trials, the risk that AVROBIO may not realize the intended benefits of our gene therapy platform, including the features of our plato® platform, the risk that our product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that we anticipate, the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical or clinical trials, will not be replicated or will not continue in ongoing or future studies or trials involving AVROBIO's product candidates, the risk that we will be unable to obtain and maintain regulatory approval for our product candidates, the risk that the size and growth potential of the market for our product candidates will not materialize as expected, risks associated with our dependence on third-party suppliers and manufacturers, risks regarding the accuracy of our estimates of expenses and future revenue, risks relating to our capital requirements and needs for additional financing, risks relating to clinical trial and business interruptions resulting from the COVID-19 outbreak or similar public health crises, including that such interruptions may materially delay our enrollment and development timelines and/or increase our development costs or that data collection efforts may be impaired or otherwise impacted by such crises, and risks relating to our ability to obtain and maintain intellectual property protection for our product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause AVROBIO's actual results to differ materially and adversely from those contained in the forward-looking statements, see the section entitled "Risk Factors" in AVROBIO's most recent Quarterly Report, as well as discussions of potential risks, uncertainties and other important factors in AVROBIO's subsequent filings with the Securities and Exchange Commission. AVROBIO explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

Investor Contact:
Christopher F. Brinzey
Westwicke, an ICR Company
339-970-2843
chris.brinzey@westwicke.com

Media Contact:
Kit Rodophele
Ten Bridge Communications
617-999-9620

krodophele@tenbridgecommunications.com

Exhibit 99.2

Disclaimer

This presentation has been prepared by AVROBIO, Inc. ("AVROBIO") for informational purposes only and not for any other purpose. Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources and AVROBIO's own internal estimates and research. While AVROBIO believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and AVROBIO makes no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. While AVROBIO believes its internal research is reliable, such research has not been verified by any independent source.

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Any forward-looking statements in this presentation are based on our current expectations, estimates and projections about our industry as well as management's current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of our product candidates, including AVR-RD-04 for the treatment of cystinosis, will not be successfully developed or commercialized; the risk that regulatory agencies may disagree with our anticipated development approach for any one or more of our product candidates; the risk of cessation or delay of any ongoing or planned clinical trials of AVROBIO or our collaborators; the risk that we may not successfully recruit or enroll a sufficient number of patients for our clinical trials; the risk that we may not realize the intended benefits of our gene therapy platform, including the features of our plato® platform; the risk that our product candidates or procedures in connection with the administration thereof, including our use of busulfan as a conditioning agent or potential use of monoclonal antibody conditioning agents, will not have the safety or efficacy profile that we anticipate; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical or clinical trials, will not be replicated or will not continue in ongoing or future studies or trials involving our product candidates; the risk that we will be unable to obtain and maintain regulatory approval for our product candidates; the risk that the size and growth potential of the market for our product candidates will not materialize as expected; risks associated with our dependence on third-party suppliers and manufacturers; risks regarding the accuracy of our estimates of expenses and future revenue; risks relating to our capital requirements and needs for additional financing; risks relating to clinical trial and business interruptions resulting from the ongoing COVID-19 pandemic or similar public health crises, including that such interruptions may materially delay our development timeline and/or increase our development costs or that data collection efforts may be impaired or otherwise impacted by such crises; and risks relating to our ability to obtain and maintain intellectual property protection for our product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause AVROBIO's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in AVROBIO's most recent Quarterly Report, as well as discussions of potential risks, uncertainties and other important factors in AVROBIO's subsequent filings with the Securities and Exchange Commission. AVROBIO explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

Note regarding trademarks: plato® is a registered trademark of AVROBIO. Other trademarks referenced in this presentation are the property of their respective owners.

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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*

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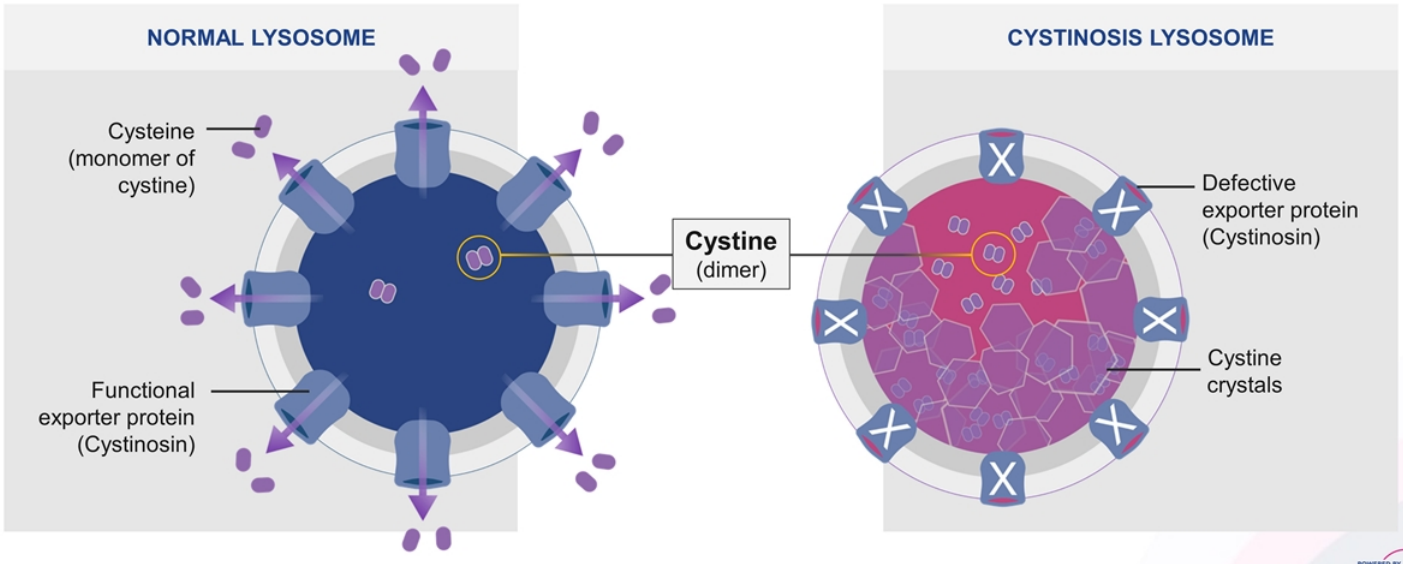
Cystinosis caused by defective gene that encodes cystinosin, an exporter protein

Cystine crystals build up in lysosomes causing tissue and organ damage



Source: Cherqui et al, Nat Rev Nephrol. 2017

CYSTINOSIS PHASE 1/2: PATIENTS 1-5

All patients continue to be oral cysteamine-independent

Patient #1 out 2 ½ years

NEW DATA

	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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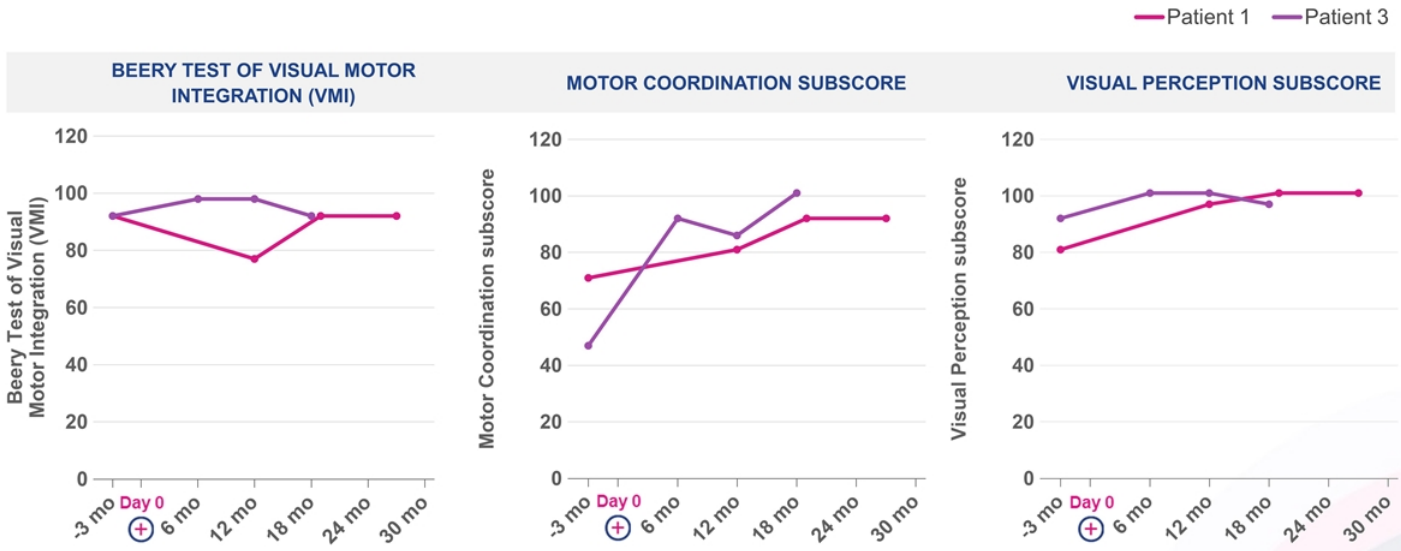
CYSTINOSIS PHASE 1/2: PATIENTS 1, 3

Improvement in motor coordination and visual perception observed post gene therapy

NEW DATA



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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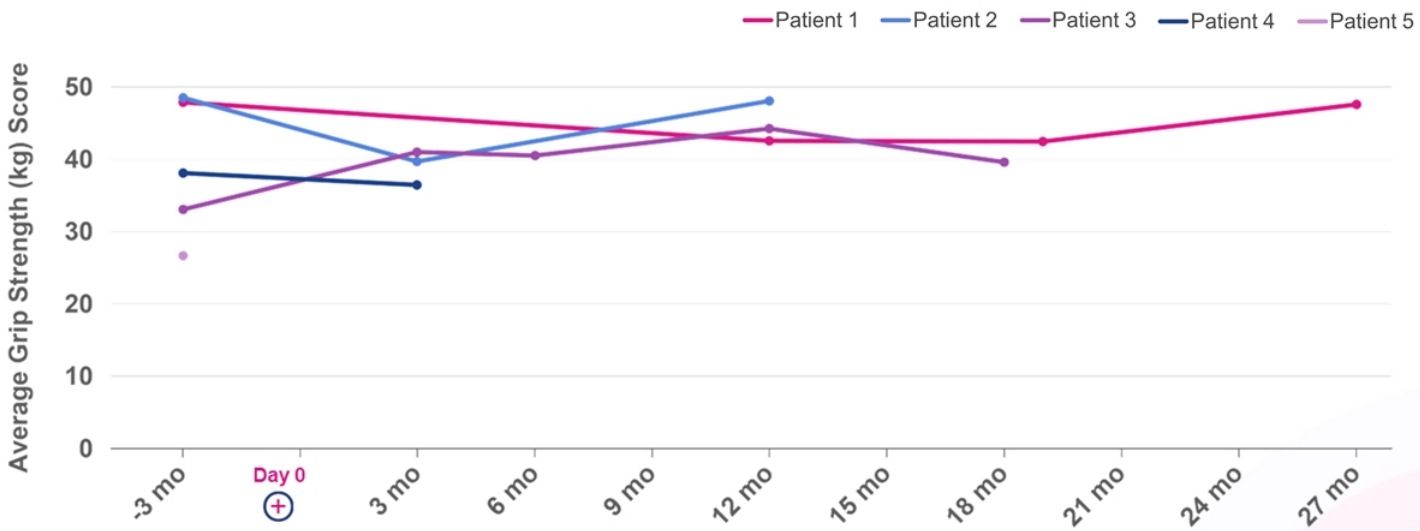
CYSTINOSIS PHASE 1/2: PATIENTS 1-5

Average grip strength stable up to 27 months

Disease progression typically leads to loss of muscle strength over time

NEW DATA



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

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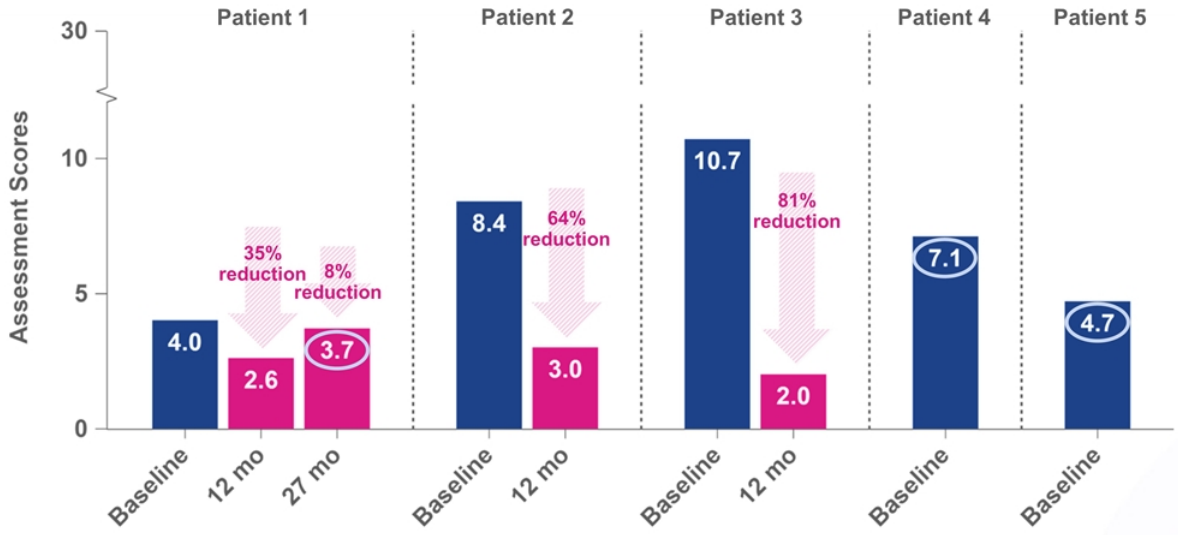
CYSTINOSIS PHASE 1/2: PATIENT 1-5

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

SKIN BIOPSY: AVERAGE INTRACYTOPLASMIC CRYSTALS PER CELL

NEW DATA POINT



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

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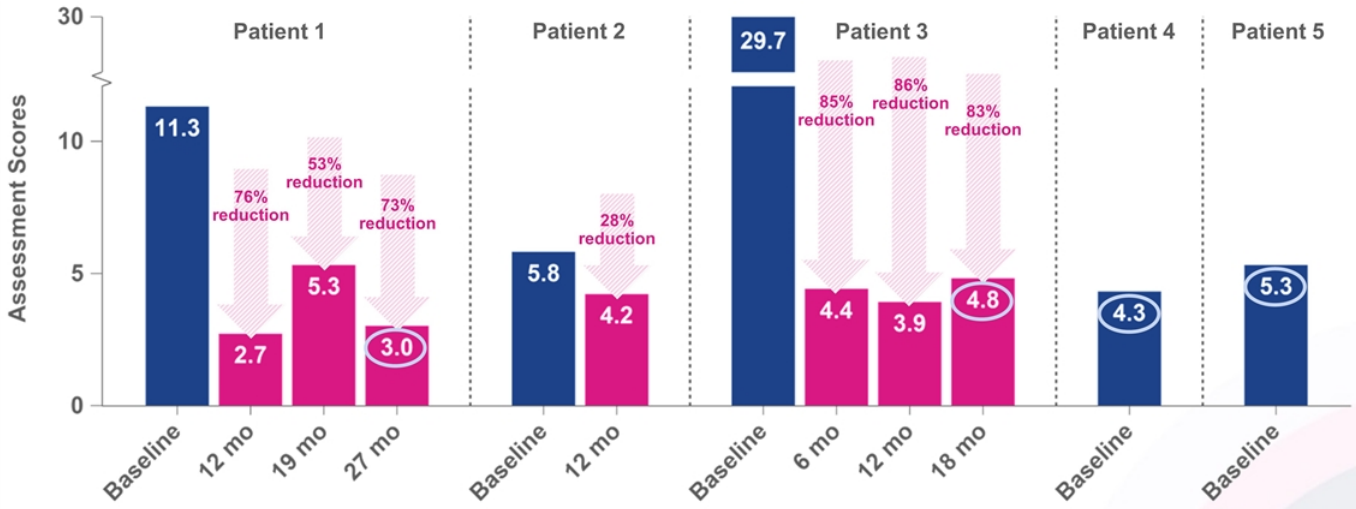
CYSTINOSIS PHASE 1/2: PATIENT 1-5

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 POINT



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

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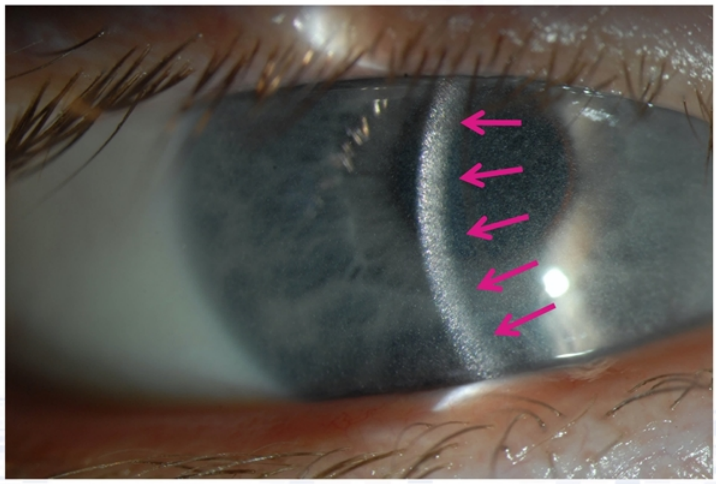
Crystal buildup in eye clearly visible before gene therapy

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



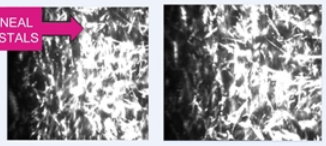
Patient 1 at baseline

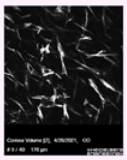
CYSTINOSIS PHASE 1/2: PATIENT 1

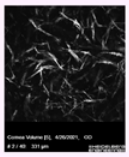
Decline in corneal crystals and improved photophobia grade

NEW DATA POINT

	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	3	*Front* of Cornea ... *Back* of Cornea	1
	174 µm, OD ... *331 µm, OD*		*176 µm, OD* ... *331 µm, OD*	







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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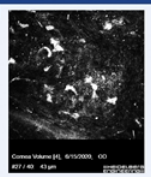
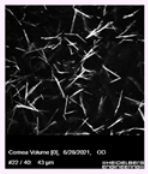
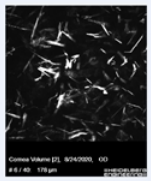
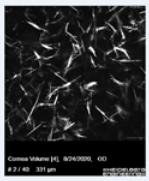
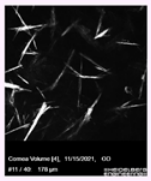
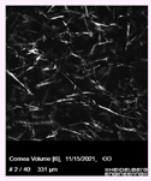
Stable corneal crystals and photophobia grade

NEW DATA

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

*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;*

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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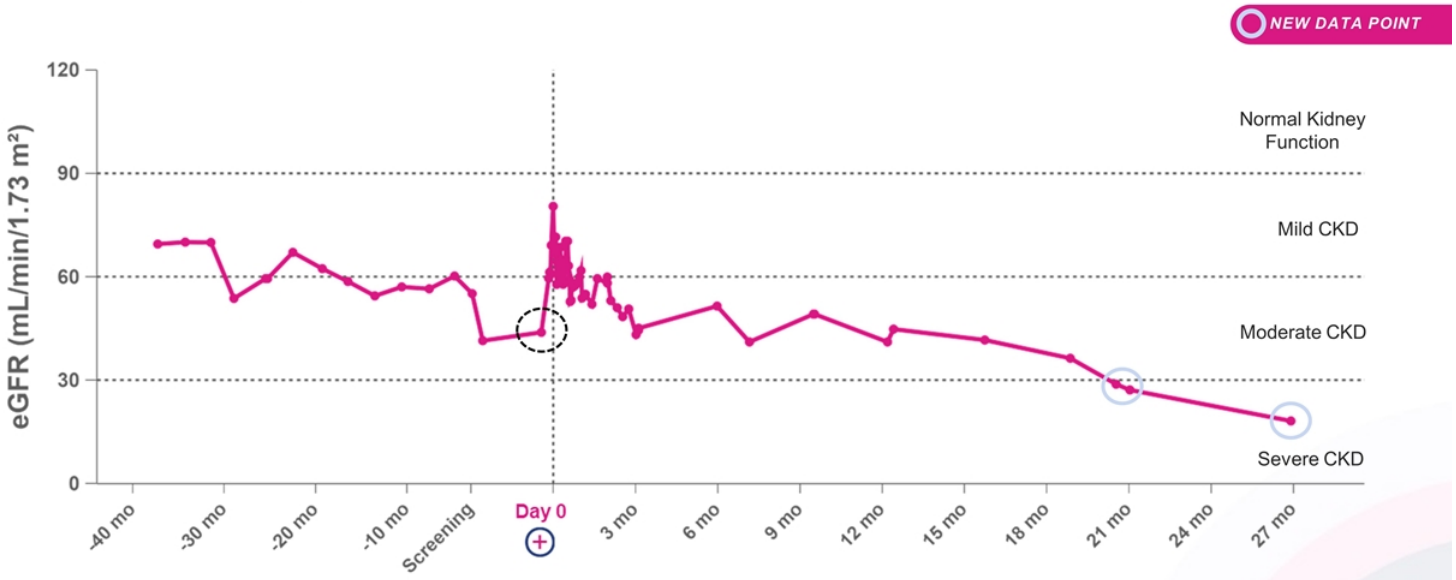
CYSTINOSIS PHASE 1/2: PATIENT 1

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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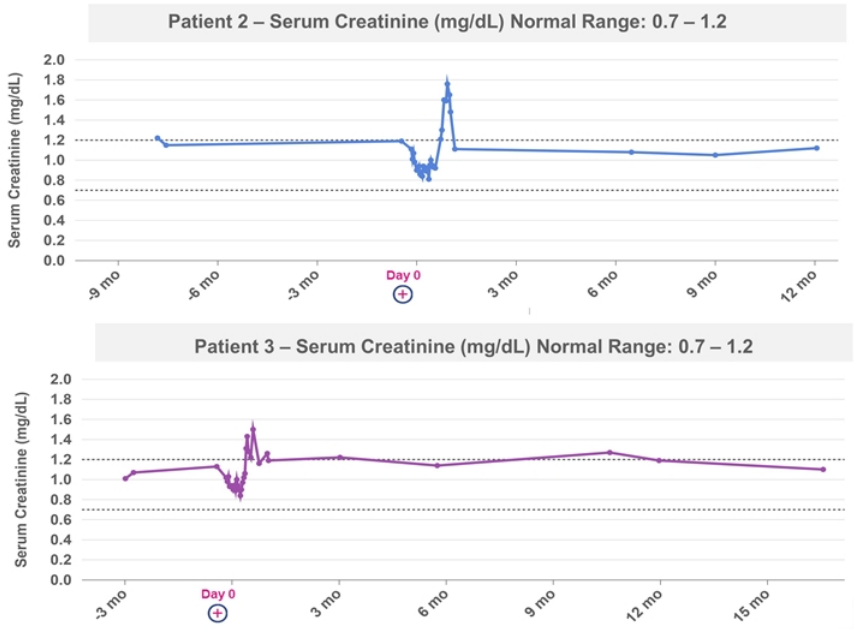
Transplanted kidney not impacted by treatment, as expected

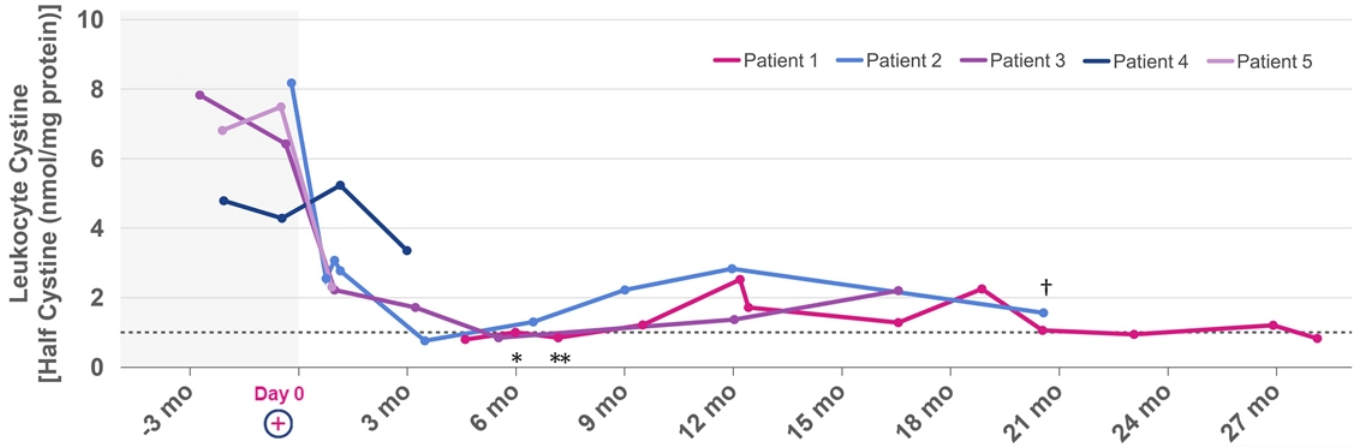
Serum creatinine remains stable post infusion

NEW DATA



Leukocyte cystine levels in blood suppressed out to 28 months

NEW DATA



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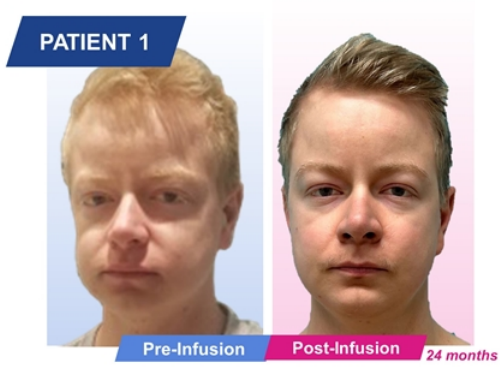
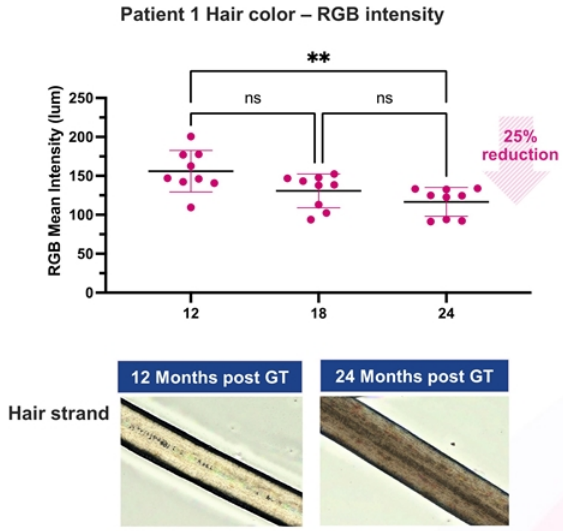
Darker pigmentation may be a sign of multi-functional cystinosin activity post gene therapy

NEW DATA

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

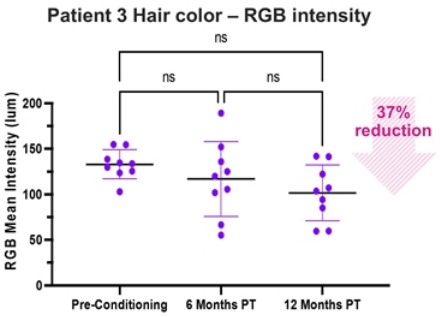
Darker pigmentation may be a sign of multi-functional cystinosin activity post gene therapy

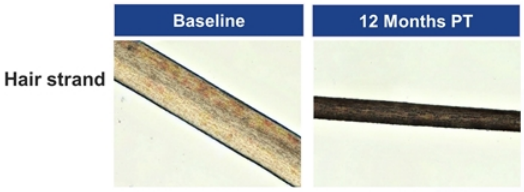
Further enforces systemic reach of gene therapy

NEW DATA

Cystinosin is located in melanosomes and regulates melanin synthesis

PATIENT 3*





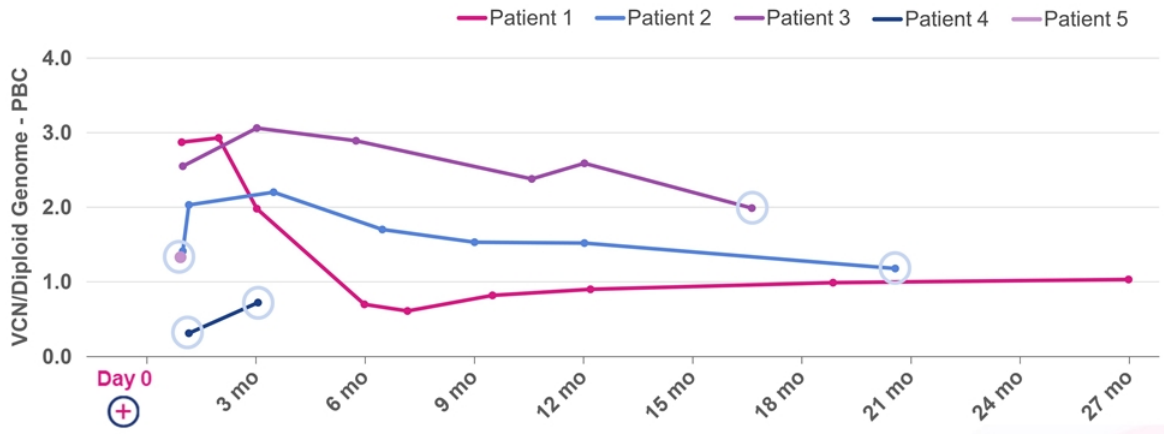
Source: Do not have permission to show patient image; Chiaverini et al., FESEB, 2012*

CYSTINOSIS PHASE 1/2: PATIENTS 1-5

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

NEW DATA POINT

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*

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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

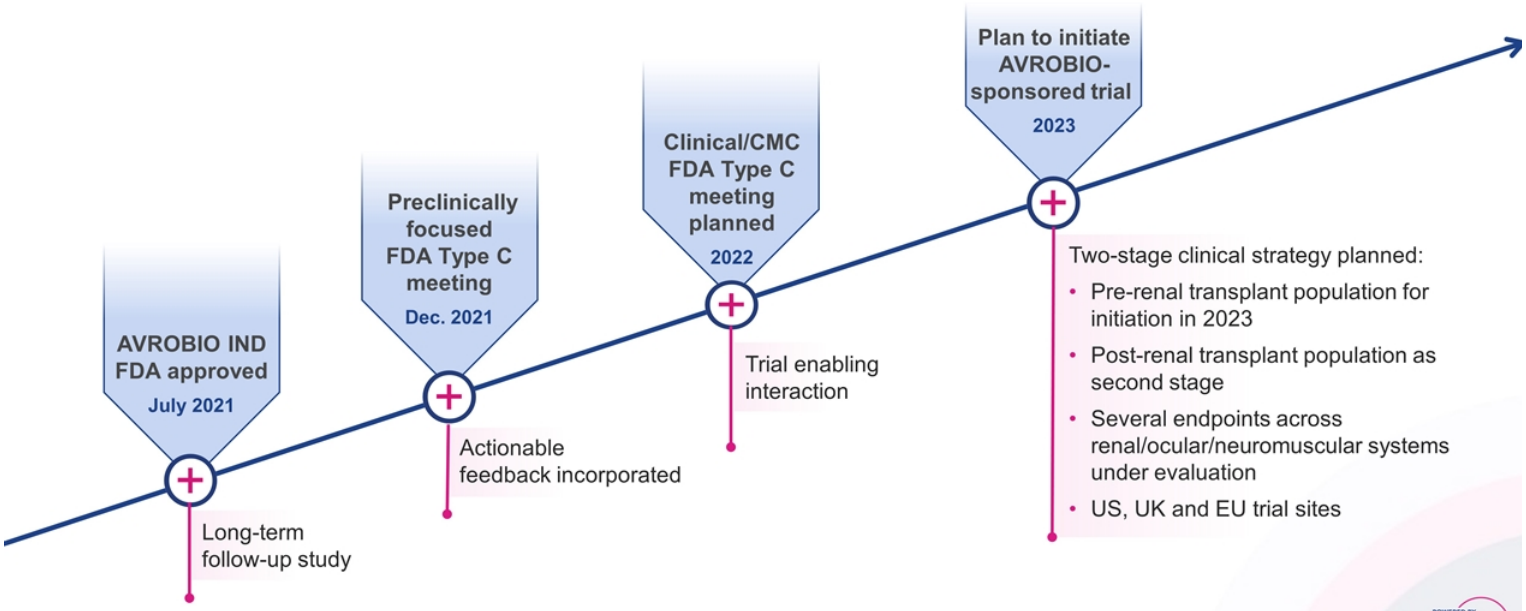
Post-treatment (not all events listed)

- 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

Building regulatory momentum

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



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*

Appendix

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

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