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): February 9, 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 February 9, 2022, AVROBIO, Inc. (the "Company") issued a press release titled "AVROBIO Reports Interim Data from Phase 1/2 Clinical Trial of Investigational Gene Therapy for Cystinosis." A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Also on February 9, 2022, the Company updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the slide presentation is furnished 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 February 9, 2022.
99.2	AVROBIO, Inc. slide presentation, dated February 9, 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: February 9, 2022

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

AVROBIO Reports Interim Data from Phase 1/2 Clinical Trial of Investigational Gene Therapy for Cystinosis

Sustained engraftment observed across first three patients 1+ year post-gene therapy; all remain off oral cysteamine to date

Reduction in number of cystine crystals as measured in skin and intestinal mucosa biopsies observed across first three patients

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 trial planned to begin in 2023

Analyst and investor conference call scheduled for today at 8:00 a.m. ET

CAMBRIDGE, Mass.—(BUSINESS WIRE)—Feb. 9, 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 interim data from a collaborator-sponsored, ongoing Phase 1/2 clinical trial[i] of AVR-RD-04, an investigational gene therapy for cystinosis, at the 18th Annual WORLD*Symposium*™ in San Diego.

The first three patients infused with AVR-RD-04 remain off oral cysteamine, with follow up durations ranging between 12- and 26-months post-gene therapy infusion. Sustained engraftment has been observed in each of these patients, as demonstrated by stable vector copy number (VCN) levels. A fourth patient was infused in November 2021. No adverse events related to the drug product have been reported in the four patients infused to date.

“The significant unmet need of people living with cystinosis remains the compelling impetus for the development of new treatments. Under existing drug regimens that are both burdensome and frequently carry substantial side effects, patients still face relentless disease progression and the prospect of debilitating symptoms, kidney transplantation with life-long immunosuppression therapy and significantly shortened lives,” said AVROBIO President and CEO, Geoff MacKay. “These interim data increase our confidence in the safety and efficacy of our gene therapy approach using the patient’s own hematopoietic stem cells and lay the groundwork for the AVROBIO-sponsored clinical trial for cystinosis planned to begin in 2023.”

Members of AVROBIO’s management team will host an Analyst and Investor conference call and webcast at 8:00 a.m. ET today to discuss the interim data update. The event can be accessed under “Events and Presentations” in the Investors section of the company’s website or by dialing 1 (866) 939-3921 from locations in the U.S. The conference ID number is 50279190. An archived recording of the event will be available on the website for approximately 30 days.

Data support engraftment and potential durability with reduction in symptoms

The collaborator-sponsored Phase 1/2 clinical trial is evaluating the safety and efficacy of AVR-RD-04 in adult patients who previously had been treated with cysteamine. AVR-RD-04 consists of the patient’s own hematopoietic stem cells, genetically modified to express functional cystinosin, the protein that is deficient in people living with cystinosis.

Interim VCN data indicate that the first three patients dosed have potentially reached a plateau 12- to 26-months post-gene therapy infusion at levels between 1 and 2.6 VCN per diploid genome (dg). VCN/dg is the average number of copies of the transgene integrated into the cell genome and is used to help assess the long-term engraftment and thus durability of gene therapy.

Skin and intestinal mucosa biopsies for the first three patients infused indicate a decline in the number of cystine crystals, with one-year reductions in average intracytoplasmic crystals per cell in skin ranging from 35% in patient 1, 64% in patient 2 and 81% in patient 3. In rectal biopsies, a 53% reduction was observed in patient 1 after 18 months, and 28% and 86% reductions were observed in patients 2 and 3, respectively, after 12 months. A hallmark of cystinosis is the accumulation of cystine in lysosomes, a type of cellular organelle, which leads to tissue and organ damage resulting in debilitating co-morbidities.

“Although this is interim data, we believe that the favorable safety profile observed to date, combined with sustained engraftment and consistent data across multiple other clinical measures, establish proof-of-concept in adult patients and support our view that gene therapy using a patient’s own hematopoietic stem cells given as a single infusion has the potential to be effective against this devastating disease,” said AVROBIO Chief Medical Officer, Essra Ridha, M.D.

Further details on the collaborator-sponsored Phase 1/2 trial (NCT03897361) of AVR-RD-04 are available on clinicaltrials.gov.

No adverse events related to drug product

Safety data from the four patients dosed to date indicate no adverse events (AEs) related to drug product. All adverse events 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.

AVROBIO-sponsored trial on track for 2023

With 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 FDA interactions this year, the company expects to initiate the AVROBIO-sponsored trial in 2023 in the U.S., followed by sites in Europe and the United Kingdom. AVROBIO’s current plan involves a two-part strategy, beginning in a pre-renal transplant population followed by a post-renal transplant population.

For more information about the collaborator-sponsored Phase 1/2 cystinosis trial and additional AVROBIO presentations at the 2022 WORLD*Symposium*™, please visit the conference website.

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, carries substantial side effects, such as breath and body odor and gastrointestinal complications, which may be difficult to tolerate, and does not prevent overall disease progression.

About AVROBIO

Our vision is to bring personalized gene therapy to the world. We aim to prevent, halt and/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 current and prospective product candidates, including AVR-RD-04 for the treatment of cystinosis, the expected safety profile of our investigational gene therapies, the design, commencement, enrollment and timing of ongoing or planned clinical trials, clinical trial results, product approvals and regulatory pathways, the timing of patient recruitment and enrollment activities, our plans and expectations with respect to interactions with regulatory agencies, timing and likelihood of success, and the expected benefits and results of our manufacturing technology, including the implementation of the plato® platform in our clinical trials and gene therapy programs and its potential impact on our commercialization activities. 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 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 on Form 10-Q, 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.

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[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).

Exhibit 99.2


AVROBIO
WORLD 2022
Cystinosis
program update
FEBRUARY 9, 2022

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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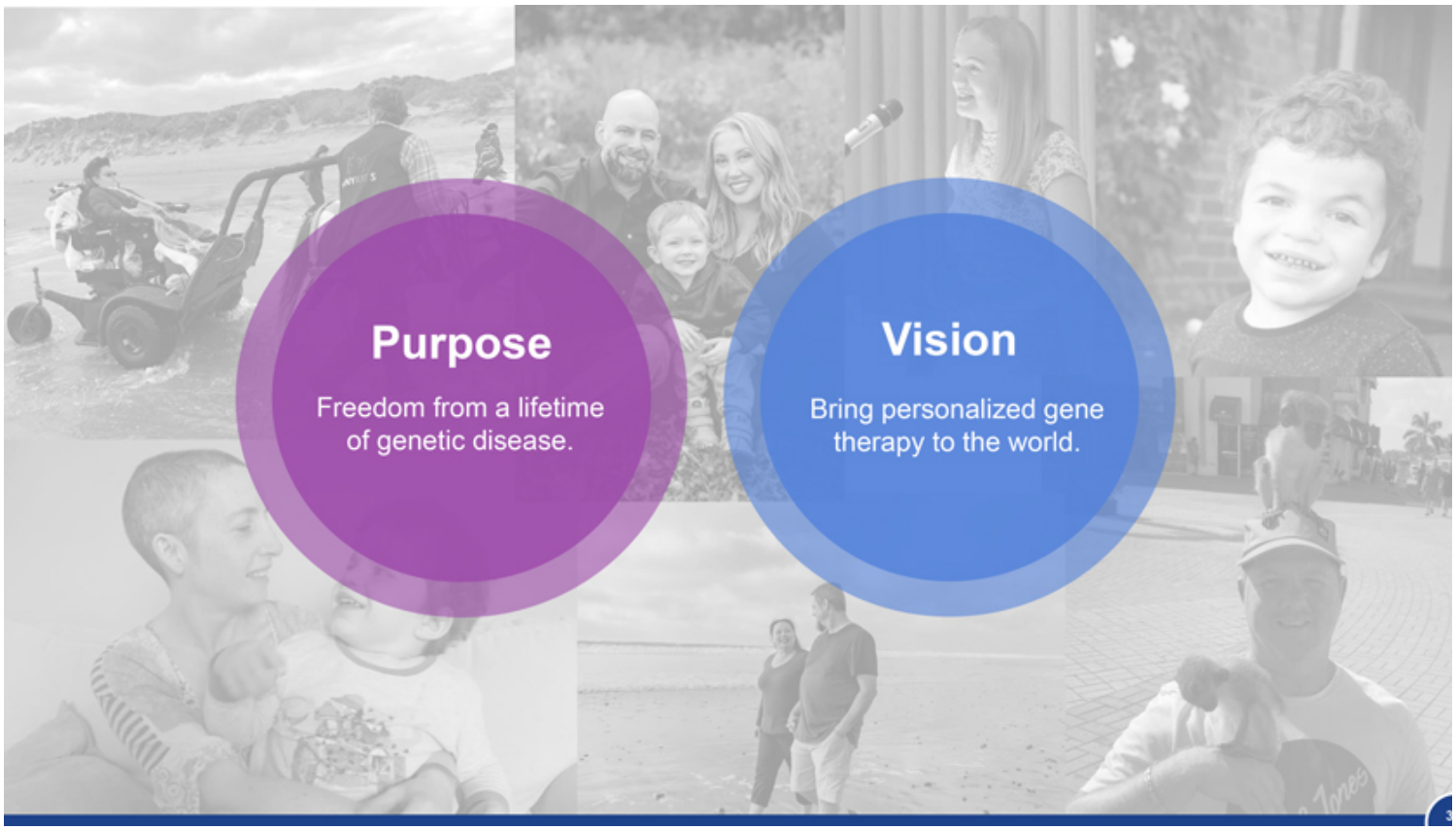
Any forward-looking statements in this presentation are based on our current expectations, estimates and projections about our industry as well as management's current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual 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 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.

AVROBIO

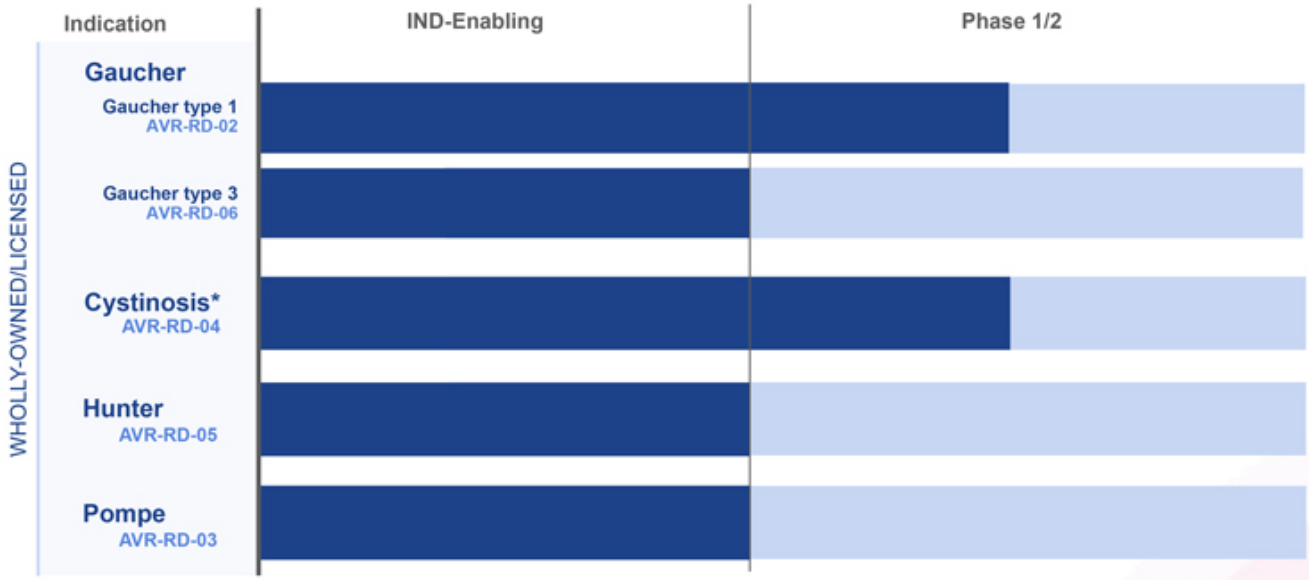

Purpose
Freedom from a lifetime of genetic disease.
Vision
Bring personalized gene therapy to the world.

Our strategy

- Build first-in-class pipeline of gene therapies using patients' own hematopoietic stem cells
- Target lysosomal disorders that require head-to-toe reach and have inadequately addressed patient needs
- Advance plato® platform to enable bringing personalized gene therapy to the world

AVROBIO

Leading lysosomal disorder gene therapy pipeline



*Planned regulatory milestones subject to regulatory agency clearance; *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).*

Multi-billion dollar market opportunity

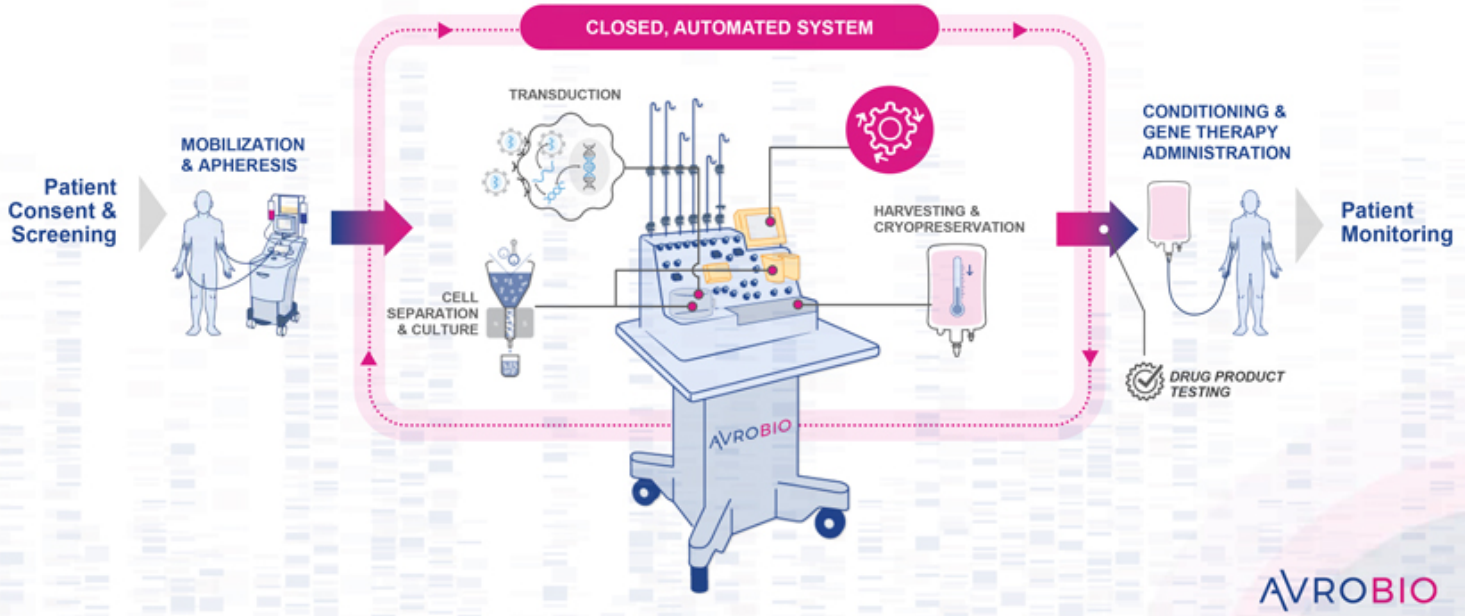
Cost of standard of care in target indications is extremely high

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

Unrivaled commercial-scale platform in plato®

End-to-end platform applied across our pipeline




Cystinosis program

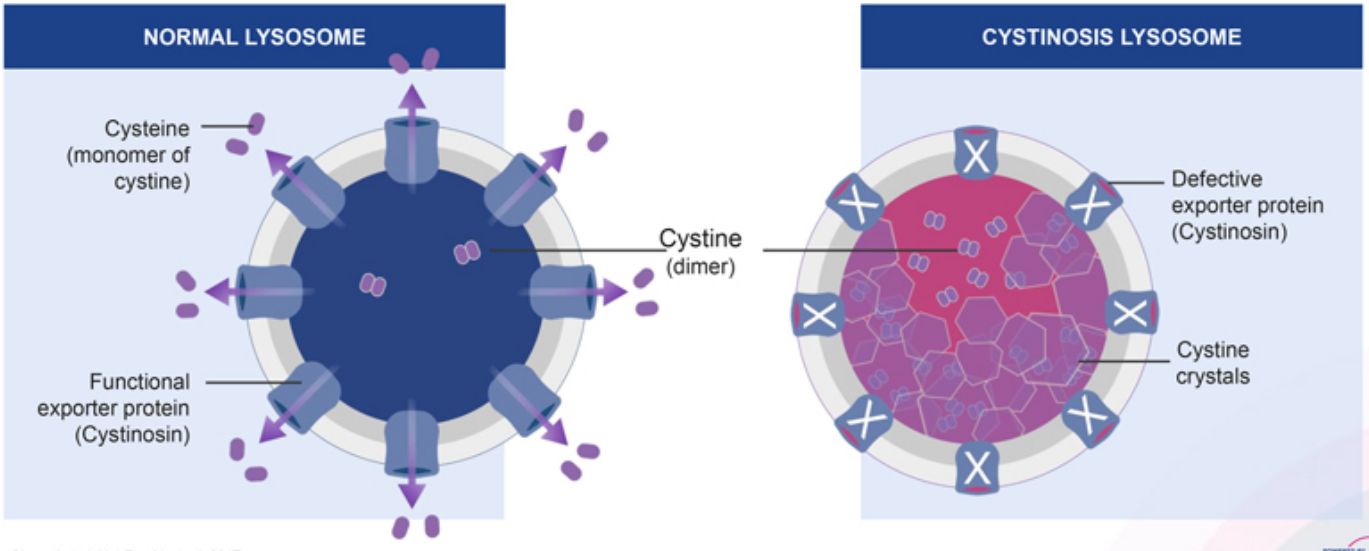
Cystinosis program update – key takeaways for today

- High unmet need – disease progression continues with SOC; lifespan significantly shortened and kidney transplant often required
- SOC is burdensome, carries substantial side effects that often lead to poor compliance and is expensive with 5-year treatment cost ~$4.3 million* in the U.S.
- Data to date demonstrate proof-of-concept in adult population in Phase 1/2 trial
  - Durable engraftment, with patient #1 off oral cysteamine for 2+ years
  - Strong, consistent data across multiple measures
  - Safety profile remains strong
- Plan to further engage with FDA later this year and begin AVROBIO-sponsored trial in 2023

*Data as of Dec. 1, 2021; 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*

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

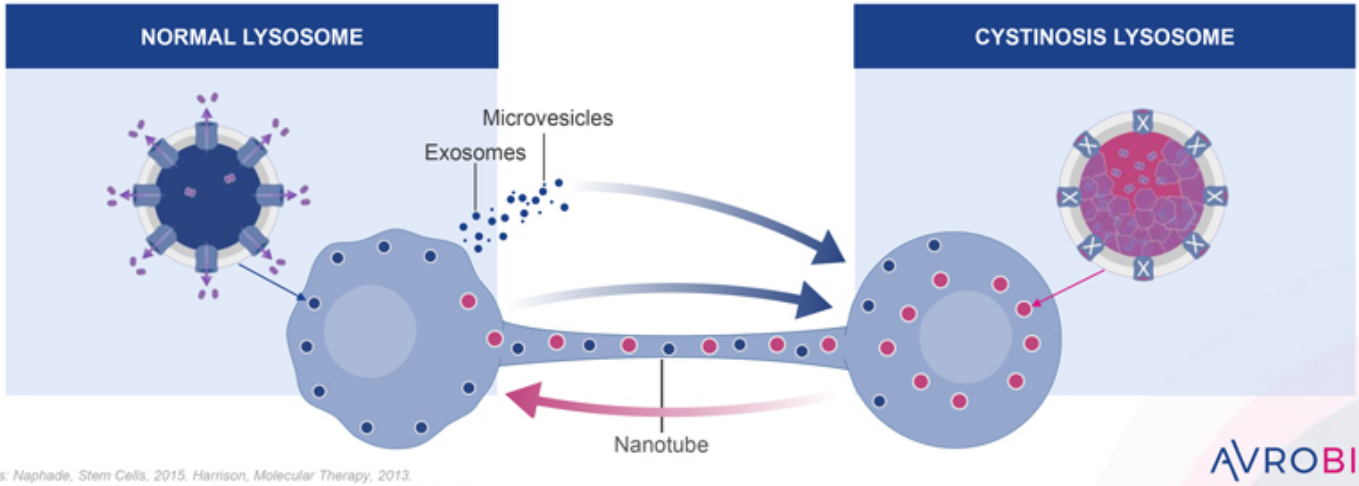
Genetically modified macrophages restore normal cystine recycling in mouse model

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

AVROBIO

Cystinosis patients are vastly underserved

Jaxon, living with cystinosis

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:

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

Vision
Corneal cystine accumulation, photophobia, involuntary eyelid closure

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

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

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

Cystinosis Target Product Profile**:

- Prevents, halts or reverses disease; extends/normalizes lifespan
- Addresses all patient segments – male & female; kidney transplant independent; all ages
- Lifelong durability – single infusion; off cysteamine pills and eye drops
- Impacts hard-to-reach organs – e.g., eye, endocrine organs, brain
- Well tolerated

Affects ~ 1:170,000 people

** WAC pricing from Redbook using standard dosing assumptions. Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate), midpoint between avg. adult and pediatric ** These are target attributes for a first-line therapy*

Treating nephropathic cystinosis patients early is essential

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.

Meet Brian, Chelsea and their sons Jaxon and Miles

AVROBIO

AVR-RD-04 collaborator-sponsored trial

PHASE 1/2
AVR-RD-04

ACTIVELY RECRUITING:

OBJECTIVES

- Safety and tolerability
- Hypothesis generation of endpoints

PATIENTS

- Up to 6 patients (4 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.

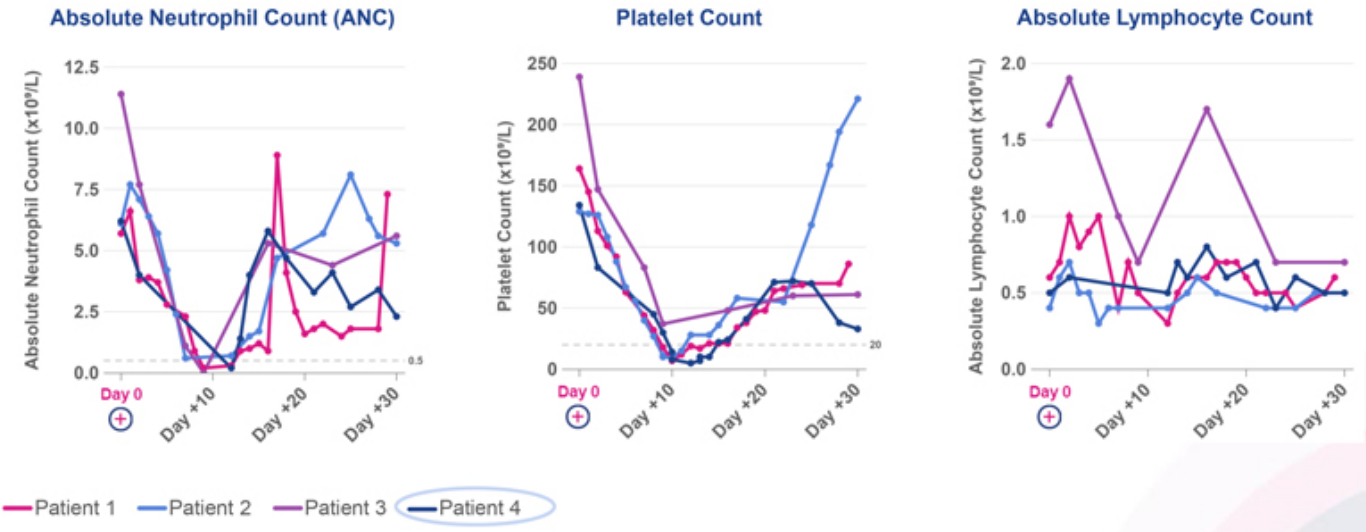
AVROBIO plato

Patient baseline characteristics

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4
Age of symptom onset/diagnosis	0 year / 8 months	0 year / 6 months	4 years	6 years
Age dosed with AVR-RD-04	20 years Infused October 2019	46 years Infused June 2020	22 years Infused November 2020	33 years Infused November 2021
Gender	Male	Male	Male	Male
Mutation	Allele 1: 57-kb deletion Allele 2: c.696dupC, p.Val233Argfs*63	Allele 1: 57-kb deletion Allele 2: c.473T>C, p.Leu158Pro	Allele 1: c.18_21del, p.Thr7Phefs*7 Allele 2: c.295_298del, p.Val99Ilefs*18	Allele 1: 57-kb deletion Allele 2: c.473T>C, p.Leu158Pro
Kidney transplant status and cysteamine dosing prior to AVR-RD-04 dosing	• No kidney transplant; stage 3 (moderate CKD) renal failure • Cysteamine 1125 mg p.o. daily • Cysteamine drops 4-5x/day	• 2 renal transplants (1987 and 1999) • Cysteamine 1800 mg p.o. daily • Cysteamine drops 6x daily	• 1 renal transplant (2010) • Cysteamine 1200 mg p.o. daily • Cysteamine drops 5x daily	• 2 renal transplants (2008 and 2017) • Cysteamine 1800 mg p.o. daily • No cysteamine drops in 2021
Manufactured AVR-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

Busulfan is transiently myeloid depleting

NEW DATA POINT

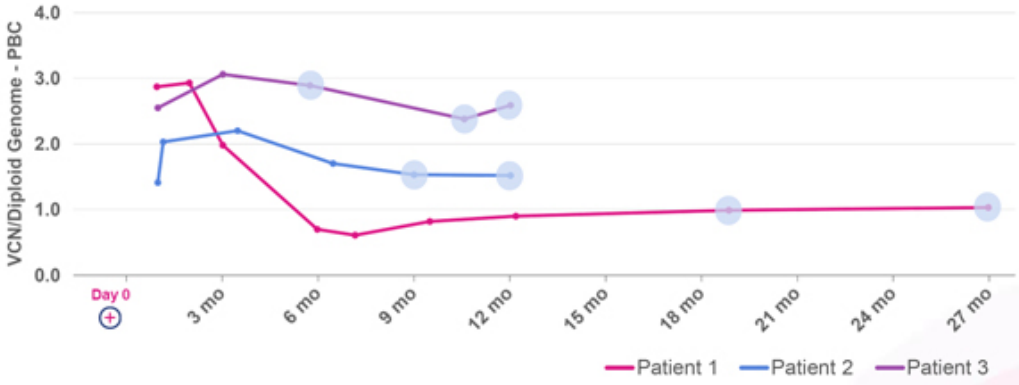


Preliminary data

Sustained engraftment to date demonstrated by VCN plateau

NEW DATA POINT

Drug Product VCN/dg	
Patient 1	2.1
Patient 2	1.3*
Patient 3	1.6



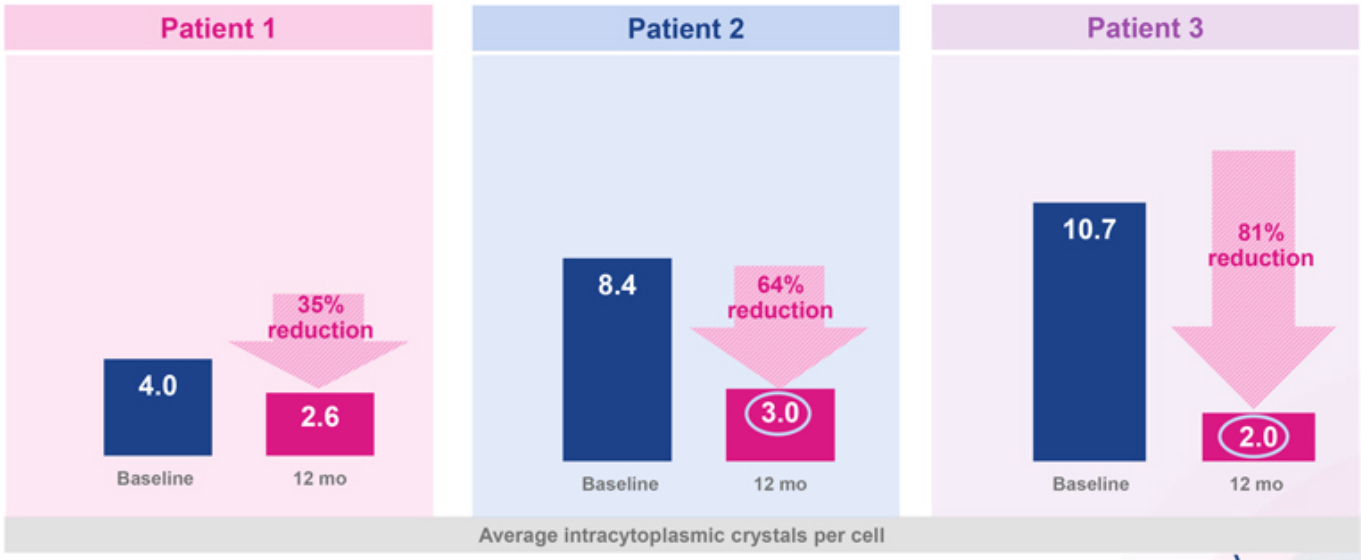
* From second apheresis
VCN: Vector Copy Number; PBCs: Peripheral Blood Cells; dg: Diploid Genome

AVROBIO

CYSTINOSIS PHASE 1/2: PATIENTS 1-3

Substantial reduction in the number of cystine crystals in skin biopsy

NEW DATA POINT

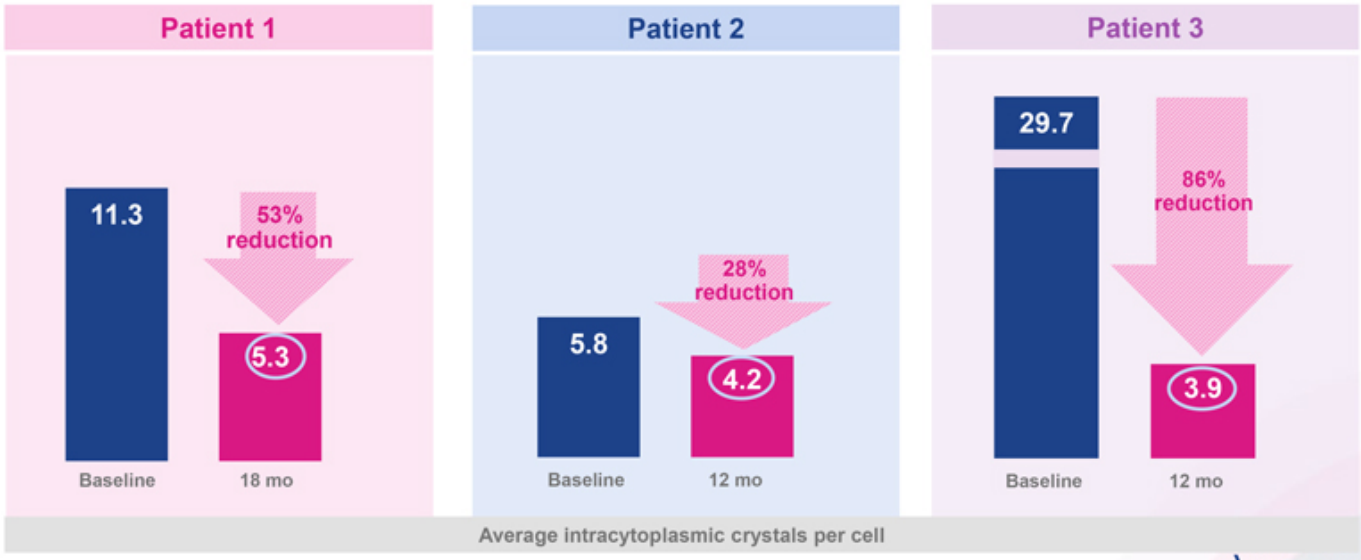


AVROBIO

CYSTINOSIS PHASE 1/2: PATIENTS 1-3

Substantial reduction in the number of cystine crystals in rectal biopsy

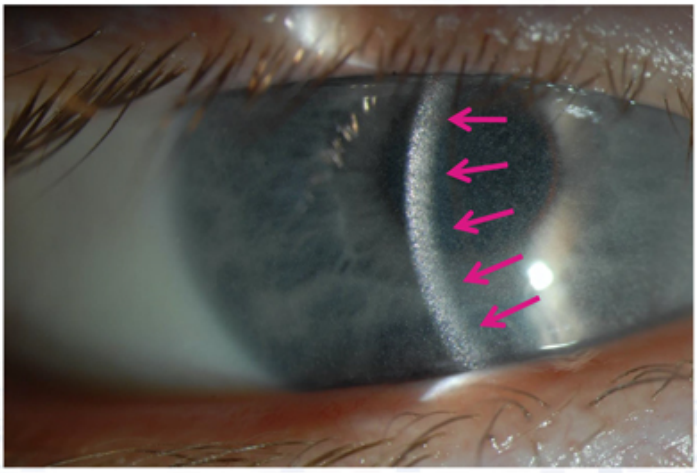
NEW DATA POINT



AVROBIO

Crystal buildup in eye clearly visible before gene therapy

Patient 1 at baseline



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Substantial decline in corneal crystals observed at 18 months

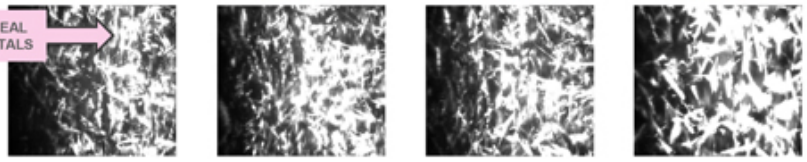
NEW DATA POINT

Front of cornea — **Back** of cornea

Baseline

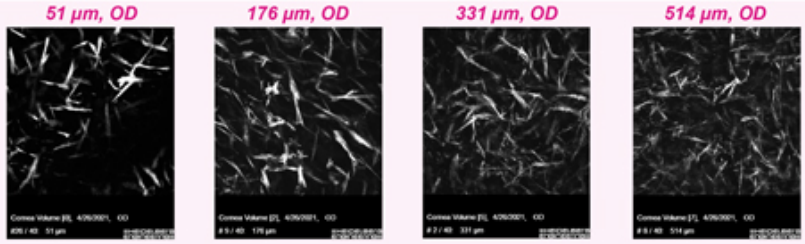
IVCM images from Nidek Confoscan

CORNEAL CRYSTALS



18 months post-gene therapy

IVCM images from Heidelberg HRT3 w/ Rostock Corneal Module



Eye layers	Right eye		Left eye	
	Baseline	12 months	Baseline	12 months
Anterior Stroma	4	3	4	1.86
Middle Stroma	4	3	4	1.71
Posterior Stroma	4	2.13	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

All patients continue to be oral cysteamine-independent

Patient #1 out 2+ years

NEW DATA

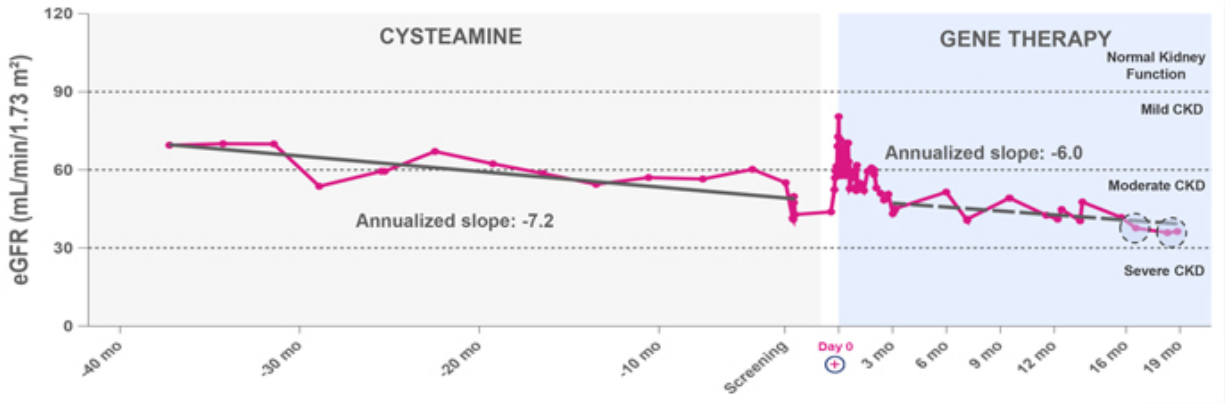
	Patient	Months off oral cysteamine and eye drops post AVR-RD-04 infusion	Current status
Oral cysteamine	PATIENT 1	26	OFF
	PATIENT 2	18	OFF
	PATIENT 3	13	OFF
Cysteamine eye drops	PATIENT 1	25	OFF
	PATIENT 2	12	ON (patient re-started July 2021)
	PATIENT 3	12	OFF

Note: Patients 2 and 3 stopped cysteamine eye drops 1-month post-transplant (per protocol); Patient 1 stopped cysteamine eye drops prior to baseline; Data as of Dec.1, 2021

eGFR data at 19 months reinforces need for early gene therapy intervention

Patient #1 with progressive CKD continues renal decline as expected

NEW DATA POINT



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Phase 1/2 Cystinosis Trial
(4 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=33 for patient 1; N=22 for patient 2; N=5 for patient 3; N=24 for patient 4
- 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

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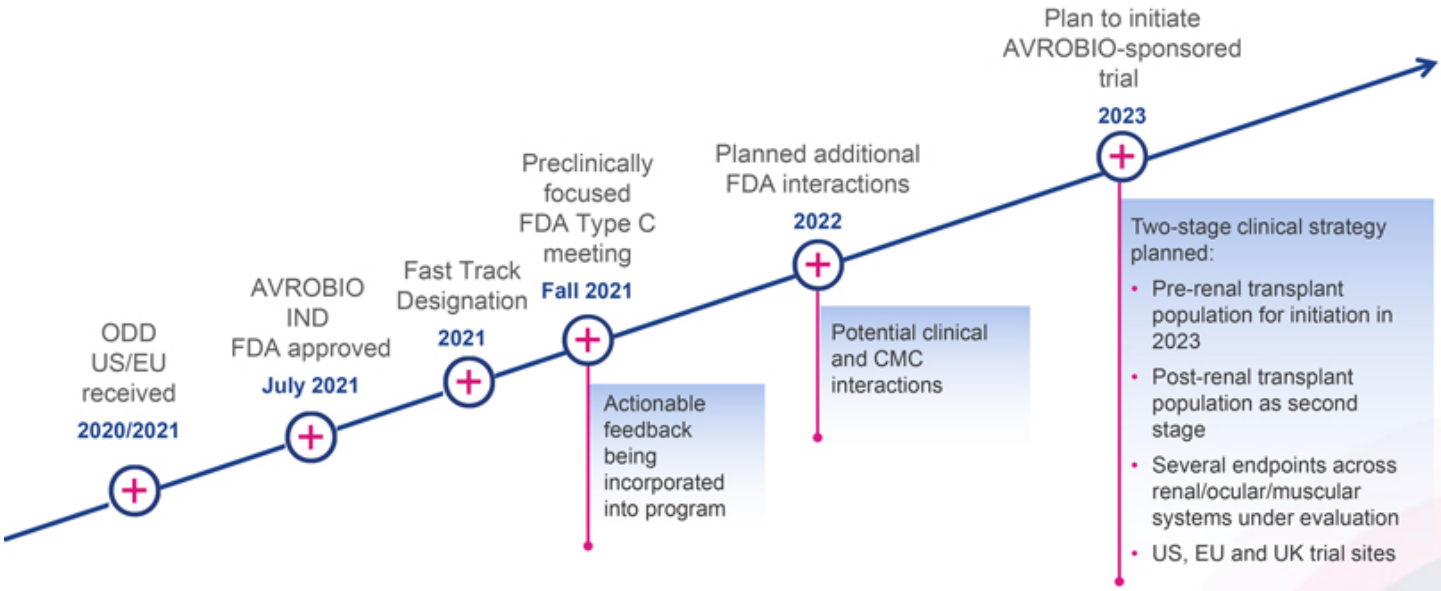
AE: Adverse Event; SAE: Serious Adverse Event; safety data cut off date is Dec. 12, 2021

Building regulatory momentum



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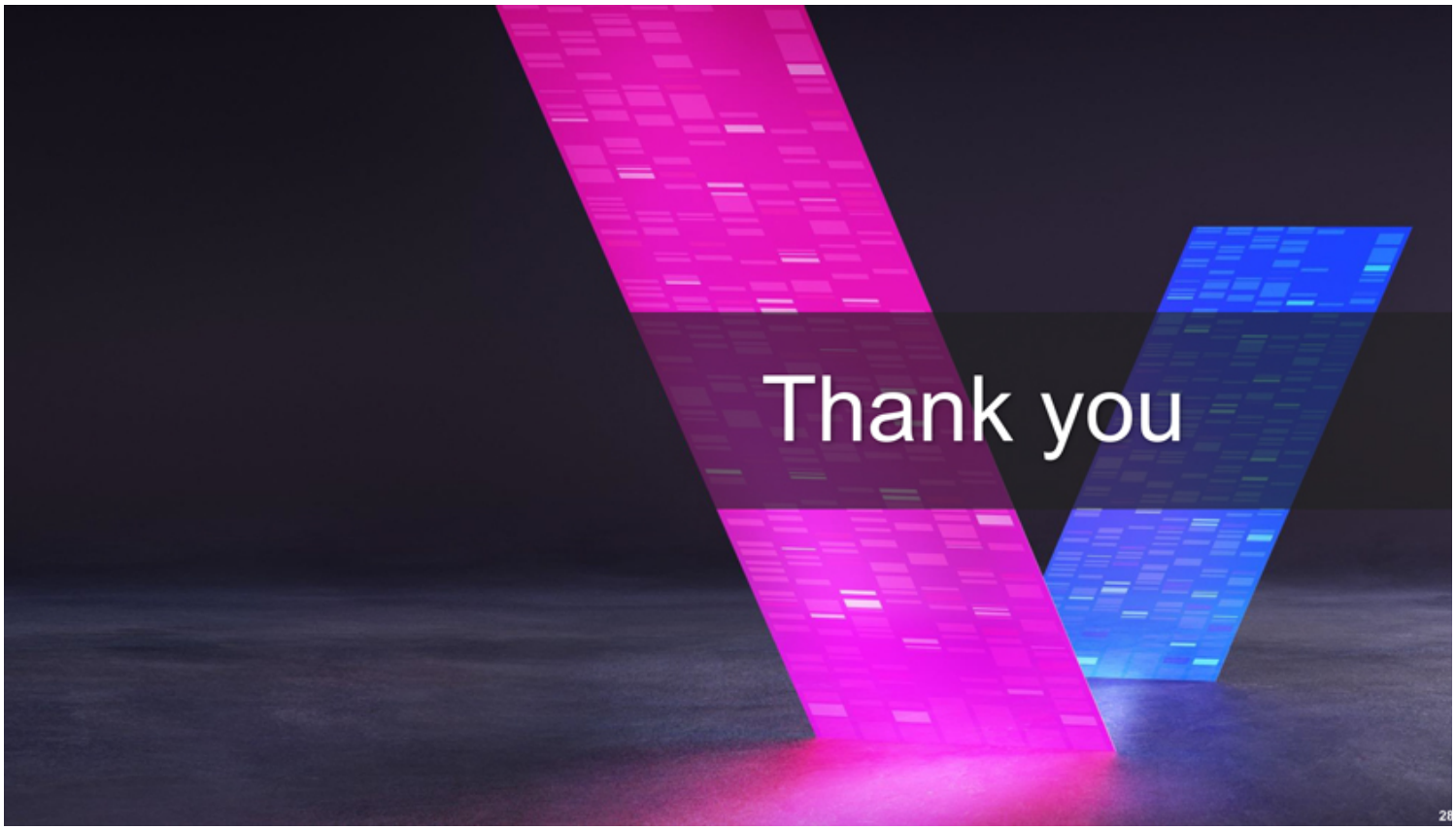
Cystinosis program update – key takeaways for today

- High unmet need – cystinosis disease progression continues with SOC; lifespan significantly shortened and kidney transplant often required
- SOC is burdensome, carries substantial side effects that often lead to poor compliance, and is expensive with 5-year treatment cost ~$4.3 million* in the U.S.
- Data to date demonstrate proof-of-concept in adult population in Phase 1/2 trial
  - Durable engraftment, with patient #1 off oral cysteamine for 2+ years
  - Strong, consistent data across multiple measures
  - Safety profile remains strong
- Plan to further engage with FDA later this year and begin AVROBIO-sponsored trial in 2023

*Data as of Dec. 1, 2021; 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*


Thank you