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 3, 2021

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 8.01 Other Events.

On May 3, 2021, AVROBIO, Inc. (the "Company") issued a press release titled "AVROBIO Provides Regulatory Update on Investigational AVR-RD-01 for Fabry Disease." A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and incorporated into this Item 8.01 by reference.

Also on May 3, 2021, 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 and incorporated into this Item 8.01 by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	AVROBIO, Inc. press release, dated May 3, 2021.
99.2	AVROBIO, Inc. slide presentation, dated May 2021.
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 3, 2021

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

Exhibit 99.1

AVROBIO Provides Regulatory Update on Investigational AVR-RD-01 for Fabry Disease

Anticipates initiating registration trial with kidney biopsy endpoint in mid-2022 to support potential full approval of AVR-RD-01 as first-line therapy, subject to FDA discussion and agreement

Two additional patients dosed in last two months in ongoing FAB-GT Phase 2 trial; plan to enroll a total of up to 14 participants

To support use of AVR-RD-01 in a broad Fabry disease population, company expects to include female patients, eliminate antibody status exclusions and collect additional cardiovascular and CNS data in FAB-GT trial

CAMBRIDGE, Mass., May 3, 2021 — AVROBIO, Inc. (Nasdaq: AVRO), a leading clinical-stage gene therapy company with a mission to free people from a lifetime of genetic disease, today provided an update on its regulatory plans for AVR-RD-01, the first investigational lentiviral gene therapy for Fabry disease. This update follows a recent U.S. regulatory development for Fabry disease therapies, as well as AVROBIO's receipt of minutes from the company's Type B (End-of-Phase 1) meeting with the U.S. Food and Drug Administration (FDA) on March 31, 2021.

On March 11, 2021, approximately three weeks before the company's End-of-Phase 1 meeting, FDA granted full approval of Fabrazyme® (agalsidase beta)[1] more than 18 years after the enzyme replacement therapy (ERT) received accelerated approval on the basis of a surrogate endpoint: reduction of GL-3 (also referred to as Gb3) inclusions in biopsied renal peritubular capillaries (PTCs). The conversion of Fabrazyme to full approval opens a new pathway for full approval of ERTs based on this surrogate endpoint, which AVROBIO believes could potentially apply to investigational AVR-RD-01. In addition, the conversion of Fabrazyme to full approval limits the accelerated approval pathways available for new therapies to treat Fabry disease. As a result, AVROBIO can no longer pursue an accelerated approval pathway for AVR-RD-01 with the FAB-GT trial as currently designed, and instead intends to discuss with FDA a registration trial with a primary efficacy endpoint of clearance of GL-3/Gb3 inclusions in biopsied renal PTCs as the basis for full approval.

"We believe we have a potential new path to pursue full approval for investigational AVR-RD-01 as a first-line therapy for Fabry disease by conducting a single, head-to-head registration trial versus Fabrazyme using a kidney biopsy surrogate endpoint similar to our FAB-GT Phase 2 trial, where we have seen 100% and 87% substrate reductions at one year post-gene therapy in the two patients with evaluable kidney biopsies," said Geoff MacKay, CEO and president of AVROBIO. "We plan to design a registration trial with a scope, size and duration comparable to other gene therapy trials."

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1 Fabrazyme® (agalsidase beta) is a registered trademark owned by Sanofi Genzyme

In its FDA briefing book, which was submitted to FDA prior to Fabrazyme's full approval, the company sought an accelerated approval pathway by expanding the FAB-GT Phase 2 clinical trial and conducting an additional confirmatory trial. The revised regulatory plan anticipates retaining the two-study approach with a similar overall requirement in terms of scope, size and duration.

The company plans to engage FDA to discuss and agree upon its revised approach, with the goal of initiating the registration trial in mid-2022. Although FDA guidance provides that a surrogate endpoint in a particular clinical development program should not be assumed to be appropriate for use in a different program, AVROBIO believes this recent development could potentially apply to investigational AVR-RD-01, a gene therapy designed to facilitate the production of functional enzyme by the patient's own stem cells after a one-time treatment with the therapeutic gene.

AVROBIO also remains on track to request a CMC-oriented Type C meeting in the second half of 2021. Additionally, in parallel the company intends to seek scientific advice from the European Medicines Agency on the planned registration trial.

Two additional patients dosed in two months, with plans to amend the FAB-GT trial protocol

The ongoing FAB-GT trial continues to progress, now with six patients dosed, including two in the past two months, and additional participants are enrolled in the trial.

To help support the use of AVR-RD-01 in a broad Fabry disease population, AVROBIO expects to amend the FAB-GT trial protocol in the second quarter of 2021 by enrolling female participants, eliminating antibody-status exclusions and adding the collection of data on additional parameters that are recognized to be limitations of ERT, such as endpoints to assess the gene therapy's potential ability to address cardiovascular and central nervous system manifestations. The company plans to enroll a total of up to 14 participants in the FAB-GT trial.

"We look forward to working with FDA and other regulators to design a single registration trial to support full approval that we hope will advance AVR-RD-01 as quickly as possible. We remain fiercely committed to our purpose: to free people living with Fabry disease from a lifetime of painful symptoms, chronic treatment and the unremitting fear of disease progression," added MacKay.

About AVR-RD-01

AVR-RD-01 is an investigational ex vivo lentiviral gene therapy designed to provide a durable therapeutic benefit for people living with Fabry disease. The therapy starts with the patient's own hematopoietic stem cells, which are genetically modified to express functional alpha-galactosidase A (AGA). Functional AGA reduces levels of globotriaosylceramide (Gb3 or GL-3), a toxic substrate, which together with its metabolite globotriaosylsphingosine (lyso-Gb3 or lyso-GL1), are associated with the signs and symptoms of Fabry disease. AVR-RD-01 has received orphan drug designations from FDA and the European Commission. AVROBIO is currently evaluating AVR-RD-01 in FAB-GT (NCT03454893), a Phase 2 clinical trial.

About Fabry Disease

Fabry disease is a rare, inherited lysosomal disorder characterized by the accumulation of globotriaosylceramide (Gb3 or GL-3) in the body's cells. The build-up of Gb3 is due to variations in the *GLA* gene, which is responsible for the production of alpha-galactosidase A, the enzyme that breaks down Gb3. When Gb3 accumulates in cells and tissues, damage may occur and result in the progressive signs and symptoms of Fabry disease, including chronic pain, gastrointestinal issues such as nausea, vomiting and diarrhea, hearing loss, heart disease, progressive kidney disease and an increased risk of stroke. Even on ERT – the current standard of care – people with Fabry disease typically have a shortened life expectancy and may experience debilitating symptoms that significantly reduce their quality of life. An estimated one in 40,000 to 60,000 males are diagnosed with Fabry disease. Fabry disease also affects females, although the prevalence is unknown.

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. Our ex vivo lentiviral gene therapy pipeline includes clinical programs in Fabry disease, Gaucher disease type 1 and cystinosis, as well as preclinical programs in Hunter syndrome, Gaucher disease type 3 and Pompe disease. AVROBIO is powered by our industry leading plato® gene therapy platform, our foundation designed to deliver gene therapy worldwide. We are headquartered in Cambridge, Mass., with an office in Toronto, Ontario. 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, our plans and expectations with respect to the development of AVR-RD-01, including timing and design of our potential registration trial, the intended use of such trial as our registration trial for this product candidate, anticipated interactions with regulatory agencies and the planned use of surrogate endpoints in future development of AVR-RD-01, results of preclinical studies, 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, and product approvals, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, timing and likelihood of success, and the expected benefits and results of our implementation of the plato® platform in our clinical trials and gene therapy programs, including the use of a personalized and ultra-precision busulfan conditioning regimen. 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 regulatory agencies may disagree with our anticipated development approach for our product candidates such as AVR-RD-01, including that we may not be able to utilize our planned registration trial of AVR-RD-01 for full approval but instead be required to conduct additional testing, that we may be required to conduct our planned testing in a more time-consuming, expensive, challenging or otherwise different manner than we envision or have conducted for our existing trials, particularly in light of the FDA's preference for clinical trials to be double-blinded and potentially include sham controls, the risk that we may not be able to utilize our envisioned surrogate endpoint to support full approval of AVR-RD-01 but instead be required to measure a different endpoint such as a clinical outcome, 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 Annual or 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.

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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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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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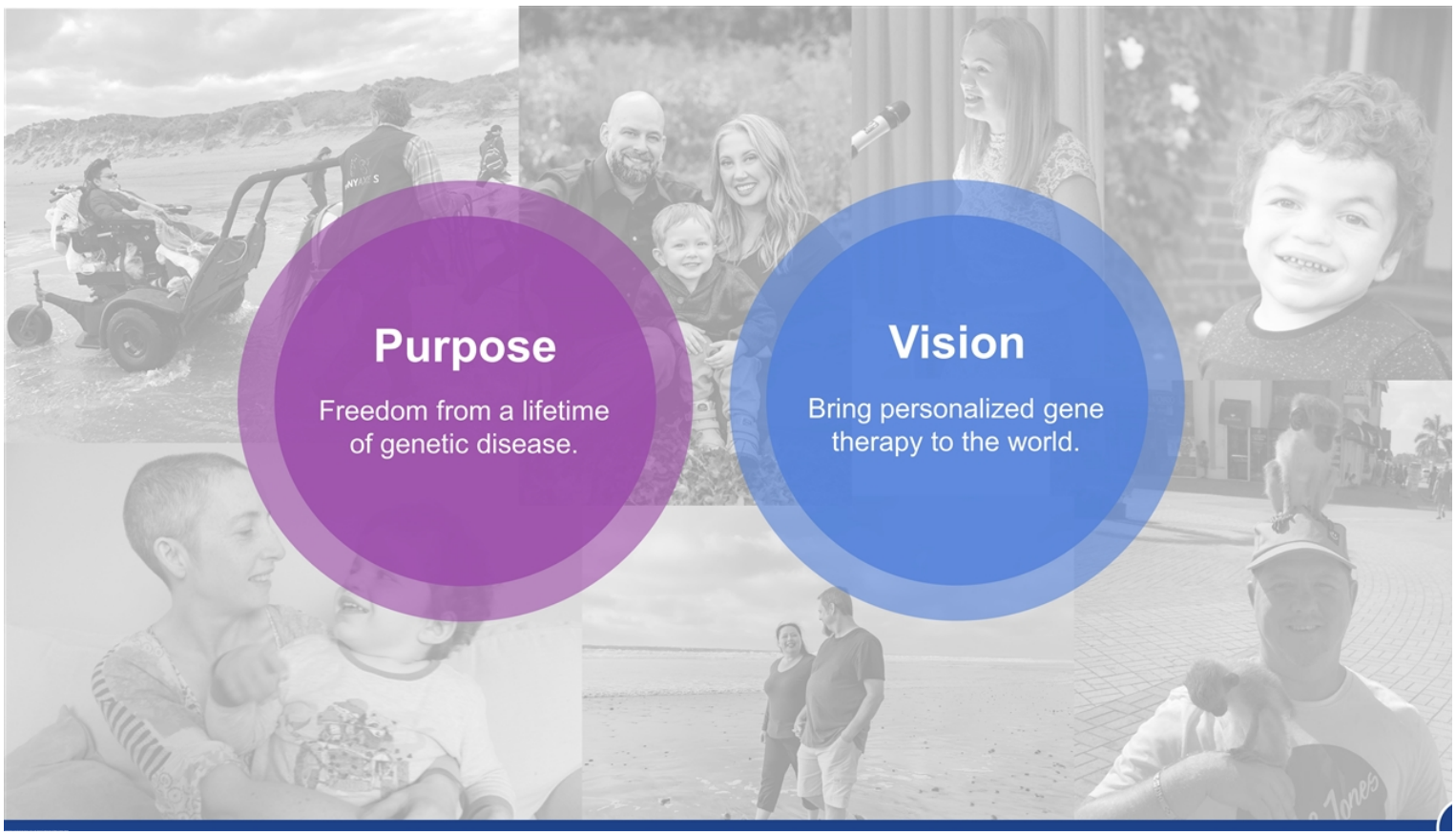
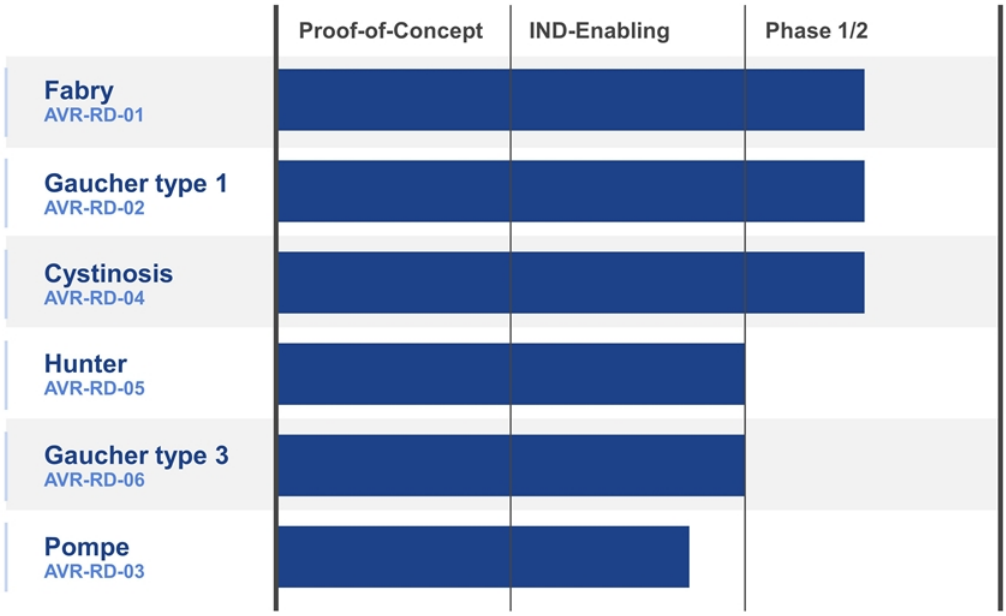

Purpose
Freedom from a lifetime of genetic disease.
Vision
Bring personalized gene therapy to the world.

Leading lysosomal disorder gene therapy pipeline

15 patients dosed to date across three indications



IND: Investigational New Drug

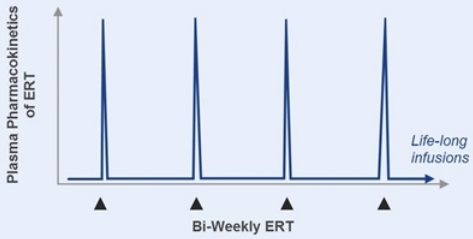
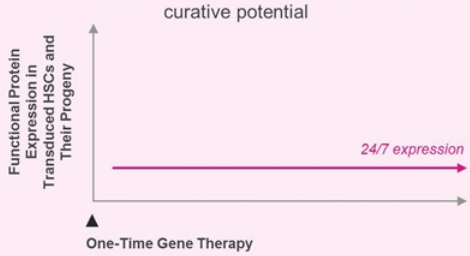
Multi-billion dollar market opportunity

Over 50,000 patients across target indications

Disease	Approx. 2020 Global Net Sales†	Five-Year SOC Cost per U.S. Patient*	Selected Companies w/ Marketed Therapies
Fabry	$1.4B	$1.7M	Sanofi Genzyme, Takeda/Shire
Cystinosis	$0.2B	$4.3M	Horizon‡
Gaucher	$1.5B	$2.3M	Sanofi Genzyme, Takeda/Shire
Hunter	$0.6B	$2.4M	Takeda/Shire
Pompe	$1.1B	$3.2M	Sanofi Genzyme
	Total: $4.8B		

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); midpoint between avg. adult and pediatric
Note: Shire acquired by Takeda in 2019
SOC: 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

Durability demonstrated across clinical programs

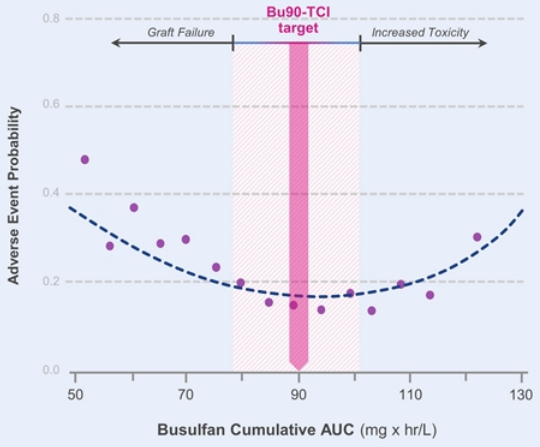
First patient out 3.5 years; 10 patients out 1 year or more

PROGRAM	PATIENT	MONTHS POST-INFUSION
Fabry Phase 1	PATIENT 1	42
	PATIENT 2	36
	PATIENT 3	24
	PATIENT 4	24
	PATIENT 5	18
Fabry Phase 2	PATIENT 1	30
	PATIENT 2	18
	PATIENT 3	18
	PATIENT 4	12
	PATIENT 5	0*
	PATIENT 6	0*
Gaucher Type 1 Phase 1/2	PATIENT 1	6
Cystinosis Phase 1/2	PATIENT 1	12
	PATIENT 2	6
	PATIENT 3	1

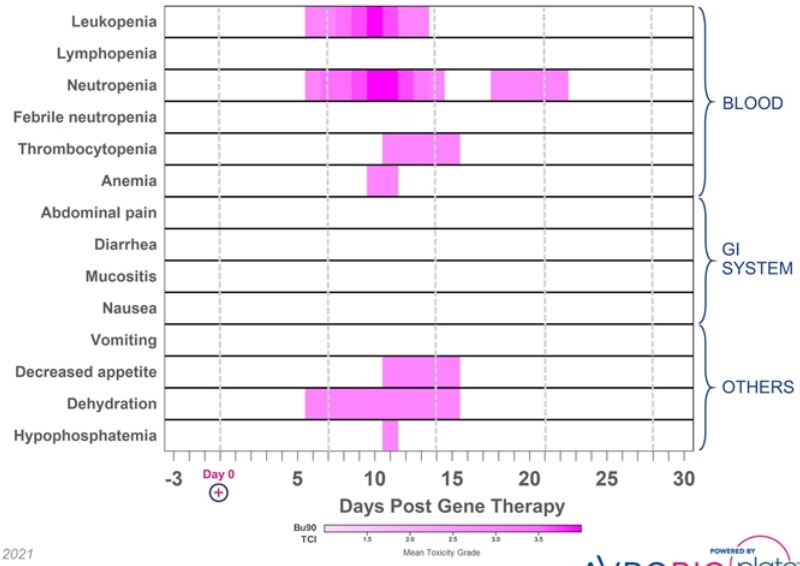
** Data not yet available for patient #5 and #6 in Fabry Phase 2*

Bu90-TCI conditioning-related side effects have been predictable and transient in first two plato® patients

Analysis of 465 non-malignant patients identified optimum exposure for busulfan conditioning:*



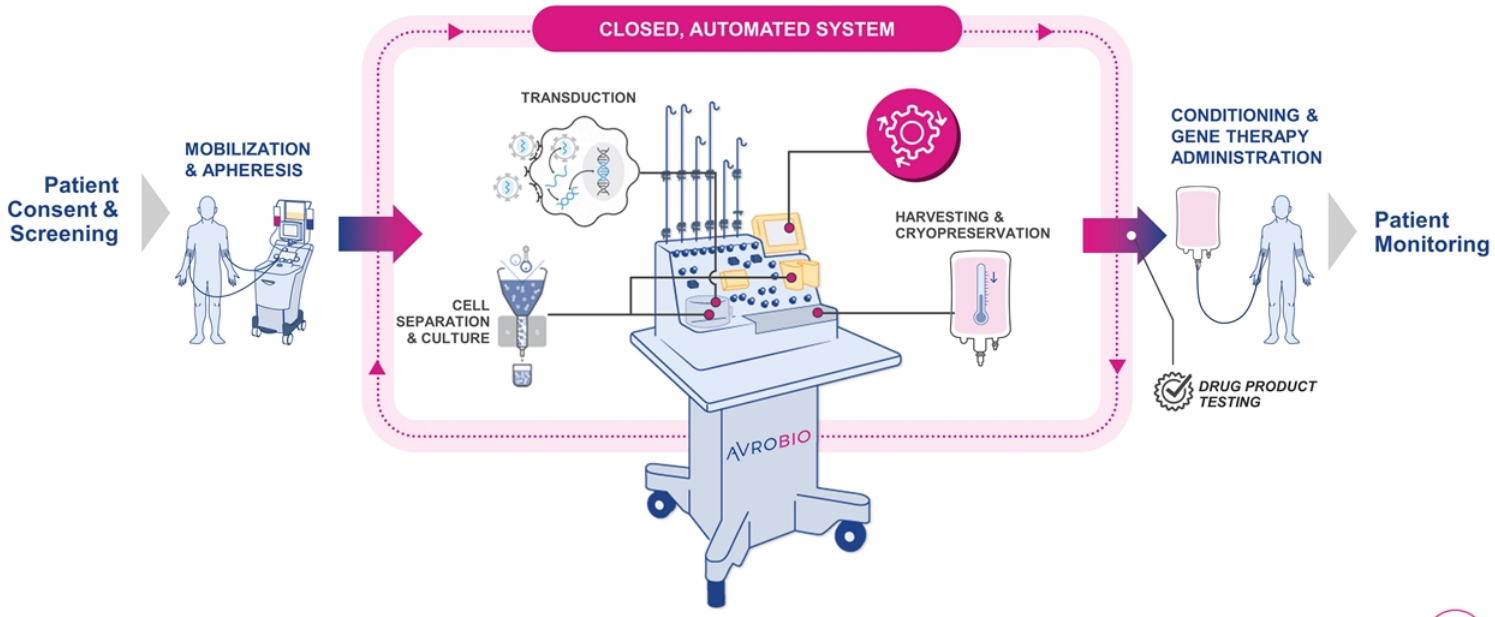
Conditioning-related grade 3-4 AEs in first two plato® patients



Note: FAB-GT, f-k-a FAB-201, safety data cut-off December 7, 2020; Gaucher safety data cut-off January 4, 2021
** Source: Bartelink IH et al., Lancet Haematol, 2016*
Bu90-TCI: Busulfan 90-Target Concentration Intervention; AUC: Area Under the Curve; TCI: Target Concentration Intervention

AVROBIO (plato) POWERED BY

Unrivaled commercial-scale platform in plato®



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“First Wave”
Programs
Fabry, Gaucher Type 1, cystinosis

Fabry disease opportunity

Tom, living with Fabry disease

Caused by mutation in gene encoding for alpha-galactosidase A enzyme

Standard of care (SOC): ERT

- Not curative, relentless progression of disease continues
- Burdensome and expensive – bi-weekly ERT infusions required; 5-year treatment cost of ERT = ~$1.7 million*

Unmet needs with SOC:

Kidney function
Proteinuria, polyuria, kidney failure

Cardiac function
Left ventricular hypertrophy, fibrosis, heart failure

Neuropathic pain
Pain and burning sensations in hands and feet, pain crises

Everyday burden of illness, and life expectancy
Not curative, relentless progression of disease, shortened lifespan

CNS complications
TIA/stroke, depression, executive function deficit, white matter lesions

Fabry Disease Target Product Profile**:

- Prevents, halts or reverses disease; extends/normalizes lifespan
- Addresses all patient segments – all genetic mutations, male and female, all ages
- Lifelong durability – single infusion; off ERT
- Impacts hard-to-reach organs – e.g., brain, heart, kidney
- Well tolerated

Affects ~ 1:40,000 males and 1:118,000 females in U.S.

** WAC pricing from Redbook using standard dosing assumptions*
*** Note: these are target attributes for a first-line therapy*

POWERED BY AVROBIO plato

Two AVR-RD-01 Fabry clinical trials

11 patients dosed across Phase 1 and 2

PHASE 1

Investigator-Sponsored Trial*

FULLY ENROLLED

OBJECTIVES	PATIENTS
• Safety and tolerability • Preliminary efficacy	• n = 5 patients • 18 – 59 year-old males • On ERT >6 months prior to enrollment

PHASE 2

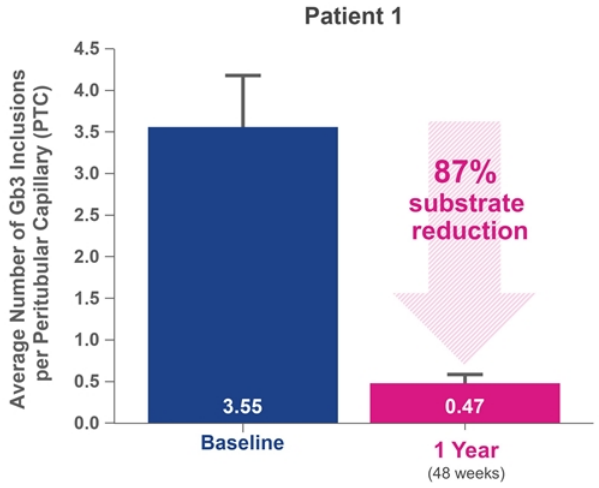
AVROBIO FAB-GT Trial **

ACTIVELY RECRUITING

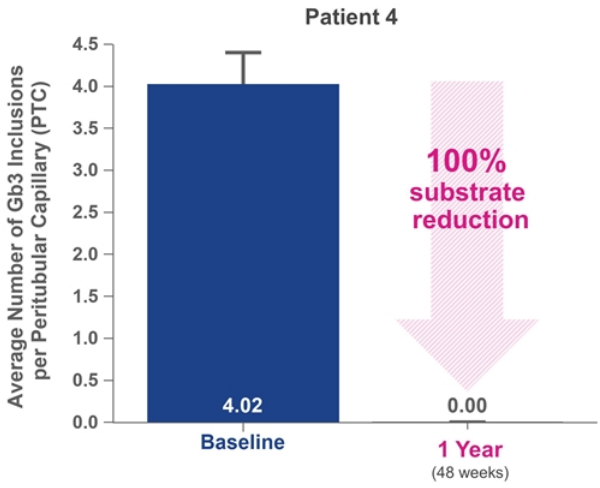
OBJECTIVES	PATIENTS
• Safety and tolerability • Efficacy	• n = 8-12 patients*** (6 dosed to-date) • 16 – 50 year-old males*** • Treatment naïve

** Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada*
*** FAB-GT fka FAB-201*
**** Plan to increase to up to 14 patients with protocol amendment, including females*

Clinically meaningful and statistically significant reduction in substrate in first two evaluable kidney biopsies



Two-sample t-test for difference between average PTCs at Baseline vs. 48 weeks; $p < 0.0001$; Error bar represents the standard error at Baseline (n=48 PTCs) and 48 weeks (n=101 PTCs). Scored by 2 independent, blinded pathologists



Two-sample t-test for difference between average PTCs at Baseline vs. 48 weeks; $p < 0.0001$; Error bar represents the standard error at Baseline (n=103 PTCs) and 48 weeks (n=99 PTCs). Scored by 2 independent, blinded pathologists

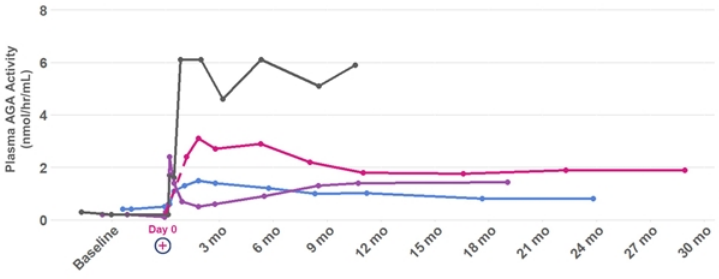
Baseline: The last available, non-missing observation prior to AVR-RD-01 infusion
Note: With respect to Fabry disease, Gb3 inclusions per PTC is interchangeable with GL-3 inclusions per KIC
PTC: Peritubular Capillary; Gb3: Globotriaosylceramide; GL-3: Globotriaosylceramide; KIC: Kidney Interstitial Capillary

FABRY PHASE 2

Durability demonstrated over multiple measures up to 2.5 years

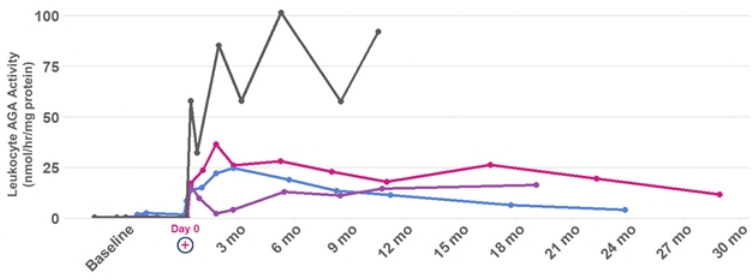
Patient 4 dosed using plato®

Plasma AGA Enzyme Activity



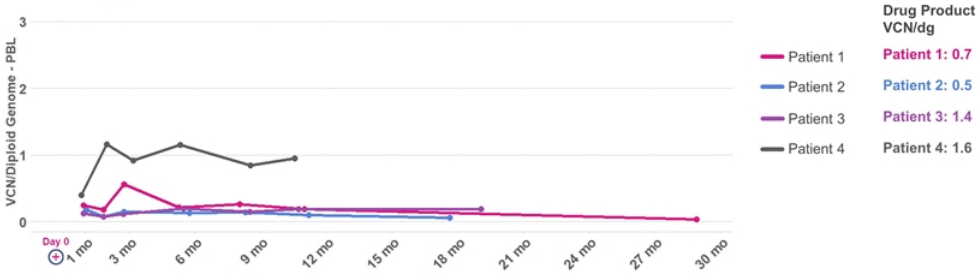
Plasma AGA Activity Reference Range: 5.1–9.2 nmol/hr/mL; AGA: α-galactosidase A

Leukocyte AGA Enzyme Activity



Leukocyte AGA Activity Reference Range: 24–56 nmol/hr/mg protein; AGA: α-galactosidase A

Vector Copy Number

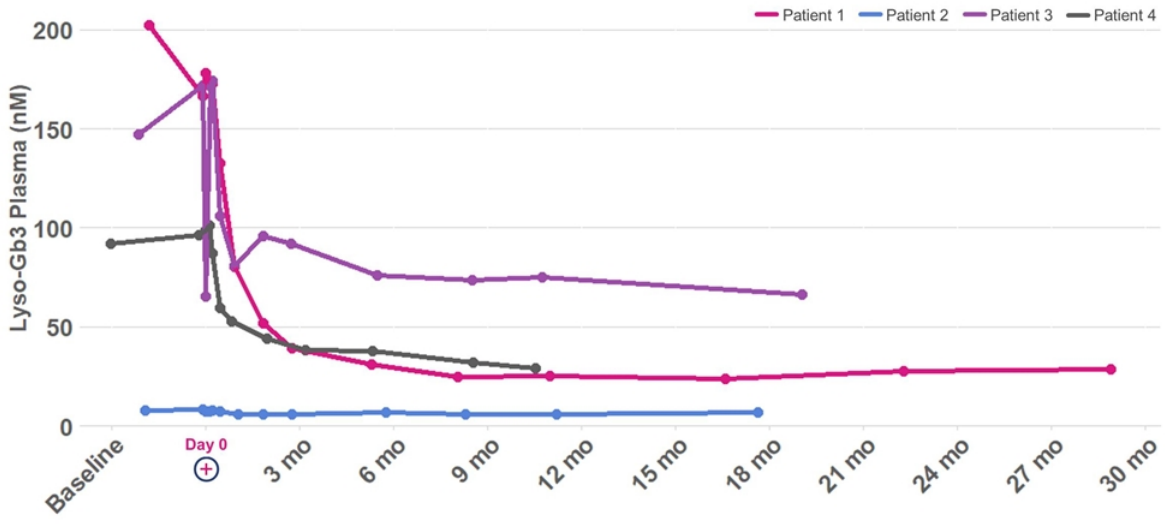


VCN: Vector Copy Number; PBL: Peripheral Blood Leukocytes; dg: Diploid Genome

AVROBIO powered by plato

FABRY PHASE 2

70% average plasma lyso-Gb3 reduction



Reduction from Baseline to Last Observation	
Patient 1	86%
Patient 2	N/A
Patient 3	55%
Patient 4	69%

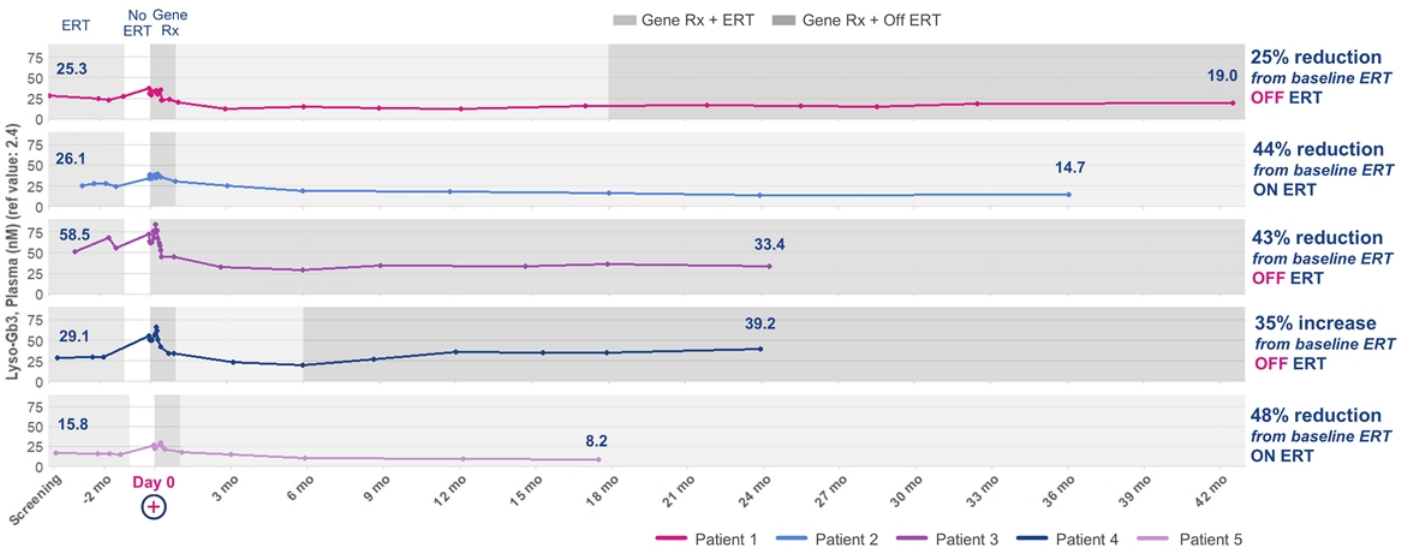
Lyso-Gb3 Plasma Reference Value: 2.4 nM; Lyso-Gb3: Globotriaosylsphingosine
Note: Patient 2 has normal substrate, consistent with late-onset cardiac variant phenotype

POWERED BY AVROBIO plato

FABRY PHASE 1

25% average plasma lyso-Gb3 reduction below baseline ERT

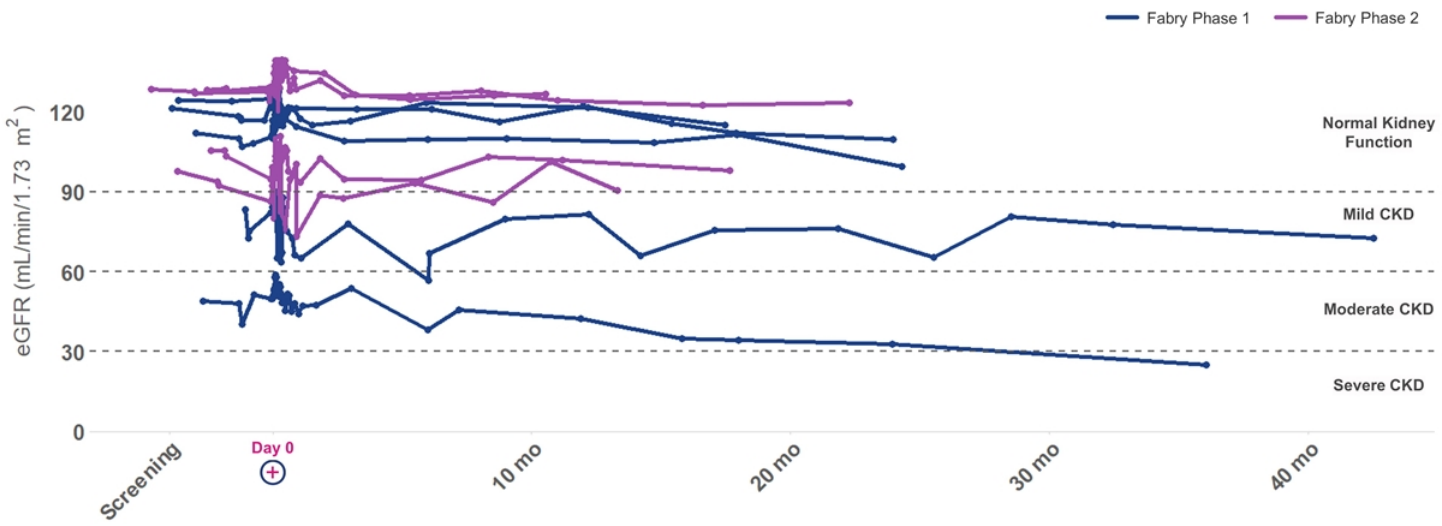
All patients who have discontinued ERT remain off ERT*



** As of January 11, 2021*

Lyso-Gb3: Globotriaosylsphingosine; ERT: Enzyme Replacement Therapy; Rx: Therapy

Kidney function (eGFR) stable up to 3.5 years*



** Eight of nine patients stable; other patient entered trial with more advanced kidney disease and a baseline eGFR level <50 mL/min/1.73m2; as expected, this patient has not stabilized, and the patient remains on ERT*

Note: eGFR was calculated using the CKD-EPI formula

eGFR: Estimated Glomerular Filtration Rate; CKD: Chronic Kidney Disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

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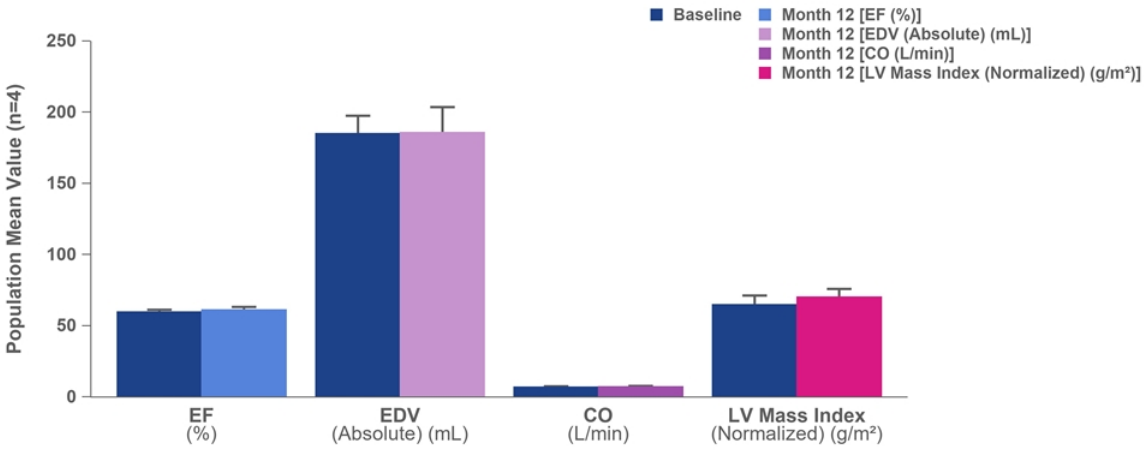
Cardiac function and mass stable across multiple measures up to 1 year



Abbreviations: EF=Ejection Fraction; EDV=End Diastolic Volume; LV=Left Ventricular.
Error bar represents the standard error of the population mean (n=4).
*Reference Range Mean Values Male 20-39 yrs; EF: 64.3 ± 4.2%; EDV: 178.6 ± 30.1 mL; CO: 4-8 L/min; LV Mass Index: 67.8 ± 10.7 g/m²
**Reference Range Mean Values Male 40-49 yrs; EF: 58-75 %; EDV: 117-200 mL; CO: 4-8 L/min; LV Mass Index: 58-91 g/m²

*Source: *Alfakih K et al, J Magn Reson Imaging, 2003 ; **Maceira AM et al, J of Cardiovascular Magnetic Resonance, 2006*

No unexpected safety events identified

Conditioning-related side effects have been manageable and transient

Phase 1 & 2 AEs and SAEs

- No AEs or SAEs related to AVR-RD-01 drug product
- AEs across trials generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions

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- Phase 1 AEs (n=94)
  - Grade 3 or 4 (n=14)
- Phase 1 SAEs (n=2) resolved without clinical sequelae
  - Post-AVR-RD-01 treatment: febrile neutropenia; thrombophlebitis

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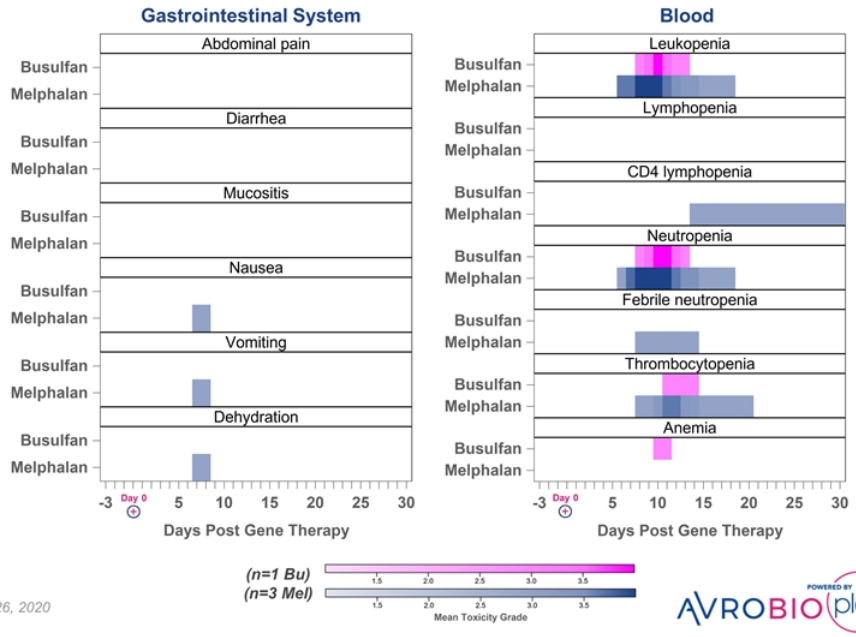
- Phase 2 AEs (n=111)
  - Grade 3 or 4 (n=22)
- Phase 2 SAEs (n=6) resolved without clinical sequelae
  - Post-AVR-RD-01 treatment: dehydration; nausea; vomiting; febrile neutropenia

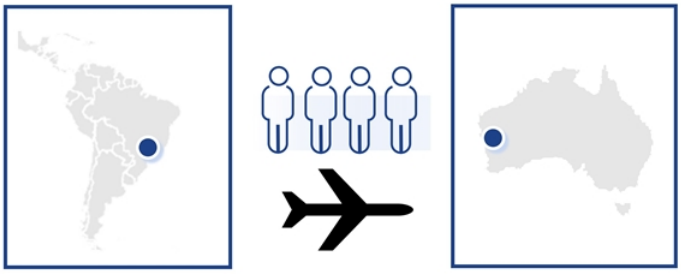
Phase 2 conditioning-related grade 3/4 AEs



Note: Phase 2 safety data cut-off December 7, 2020; Phase 1 safety data cut-off November 26, 2020
AE: Adverse Event; Bu: Busulfan; Mel: Melphalan

Accelerating enrollment by adding international referrals

TWO Fabry patients from Brazil have been dosed and
TWO additional patients enrolled in Australia



Long-term follow-up expected
to take place in Brazil

Global patient recruitment

- Expands pool of potential patients
- Helps navigate COVID-19 issues
- First global center of excellence established in Australia

Regulatory update on AVR-RD-01

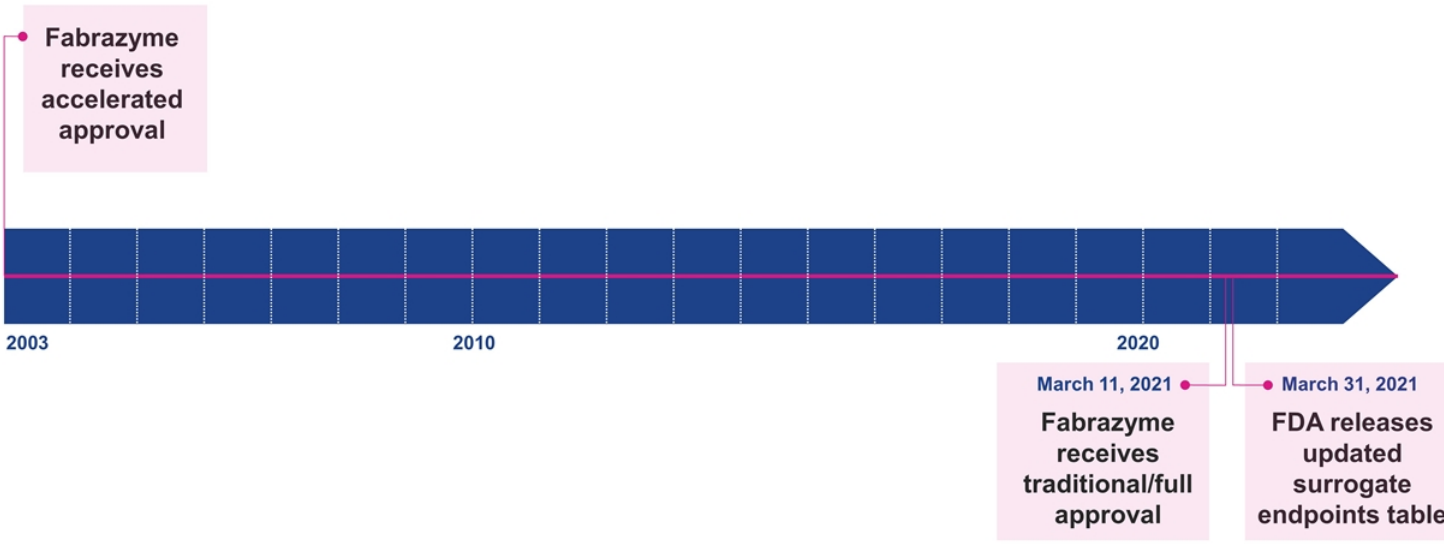
- Just prior to our End-of-Phase 1 meeting with the FDA, Fabrazyme® was converted from accelerated to full approval based upon a kidney biopsy surrogate endpoint
- We believe this development opens a new pathway for the potential full, traditional approval of AVR-RD-01
- We plan to design a single head-to-head registration trial versus Fabrazyme with a scope, size and duration comparable to other gene therapy trials, using a kidney biopsy surrogate endpoint similar to our FAB-GT Phase 2 trial
- Our briefing book submitted to FDA (prior to Fabrazyme full approval) proposed an expanded Phase 2 clinical trial and an additional confirmatory trial
  - Revised regulatory plan similarly anticipates a two study approach with a similar overall requirement in terms of scope, size and duration

PLANNED NEXT STEPS:

- Request clinically-oriented Type C meeting with FDA to discuss and seek agreement on revised approach
- Request CMC-oriented Type C meeting with FDA in second half of 2021
- Amend FAB-GT Phase 2 protocol to collect data on additional parameters that are recognized to be limitations of ERT and cap enrollment at up to 14 patients
- Initiate registration trial in mid-2022

FDA: Food and Drug Administration

FDA conversion of Fabrazyme to traditional approval impacts approval pathways for future Fabry treatments



FDA: Food and Drug Administration

Updated FDA table of surrogate endpoints (as of 3/31/21)

Table of Surrogate Endpoints That Were the Basis of Drug Approval or Licensure | FDA

Disease or Use	Patient Population	Surrogate endpoint	Type of approval appropriate for	Drug mechanism of action
Diphtheria vaccine (in combination vaccines)	Persons to be immunized against diphtheria	Anti-diphtheria toxoid antibody	Traditional	Induction of immunity
Duchenne muscular dystrophy (DMD)	Patients with DMD who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping	Skeletal muscle dystrophin	Accelerated	Antisense oligonucleotide
Exocrine pancreatic insufficiency	Patients with exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions	Fecal coefficient of fat absorption	Traditional	Combination of porcine-derived lipases, proteases, and amylases
Fabry disease	**Patients with confirmed Fabry disease**	**Complete/near complete clearance of GL-3 inclusions in biopsied renal peritubular capillaries (using the Fabrazyme Scoring System)**	**Traditional**	**Enzyme replacement therapy**
Fabry disease	Patients with confirmed Fabry disease and amenable *GLA* gene variants	Reduction of GL-3 inclusions in biopsied renal peritubular capillaries (using the BLISS methodology)	Accelerated	Pharmacological chaperone
Female hypogonadotropic hypogonadism	Infertile women with hypogonadotropic hypogonadism	Follicle size, serum estradiol and progesterone#	Traditional	Gonadotropin
First aid antiseptic; Health care antiseptic; Consumer antiseptic	General public, consumers, and health care professionals	Bacterial count	Traditional and Monograph	Antimicrobial
Gout	Patients with gout	Serum uric acid	Traditional	Xanthine oxidase inhibitor; URAT1 inhibitor; Uricase
Hepatitis A (Hep A) vaccine	Persons to be immunized against Hep A	Anti-Hep A antigen antibody	Traditional	Induction of immunity
Hepatitis B (Hep B) vaccine	Persons to be immunized against Hep B	Anti-Hep B antigen antibody	Traditional	Induction of immunity
Hepatitis B Virus (HBV)	Patients with HBV infection with or without cirrhosis	Undetectable plasma HBV-DNA for indefinite treatment or HBsAg loss for finite treatment	Traditional	Antiviral
Hepatitis C Virus (HCV)	Patients with HCV infection with or without cirrhosis	Sustained viral response (HCV-RNA)	Traditional	Antiviral
Hepatitis D Virus (HDV)	Patients with HDV infection with or without cirrhosis	≥ 2 log reduction in HDV-RNA plus normalization of ALT or HDV below the LLOQ*	Accelerated	Antiviral
Hepatorenal syndrome	Patients with hepatorenal syndrome type 1	Serum creatinine*	Traditional	Mechanism agnostic*
Homozygous sitosterolemia (phytosterolemia)	Patients with homozygous sitosterolemia (phytosterolemia)	Plasma sitosterol and campesterol	Traditional	Dietary cholesterol absorption inhibitor

FDA: Food and Drug Administration
Note: FDA guidance provides that the acceptability of a surrogate endpoint in a particular clinical development program should not be assumed to be appropriate for use in a different program.

Cystinosis opportunity

Jaxon, living with cystinosis

Caused by CTNS gene defect, resulting in cystine buildup in lysosomes

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

- Not curative, relentless progression of disease continues; significantly shortened lifespan; kidney transplant often required
- Burdensome and expensive – high pill burden and hourly eye drops; 5-year treatment cost 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*
*** Note: these are target attributes for a first-line therapy*

POWERED BY AVROBIO plato

Steady enrollment in AVR-RD-04 IST trial in cystinosis

PHASE 1/2
AVR-RD-04

ACTIVELY RECRUITING:

OBJECTIVES	PATIENTS
• Safety and tolerability • Hypothesis generation of endpoints	• Up to 6 patients (3 patients enrolled 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; IST does not use plato® platform
Note: AVR-RD-04 aka CTNS-RD-04
IST: Investigator Sponsored Trial

AVROBIO powered by plato

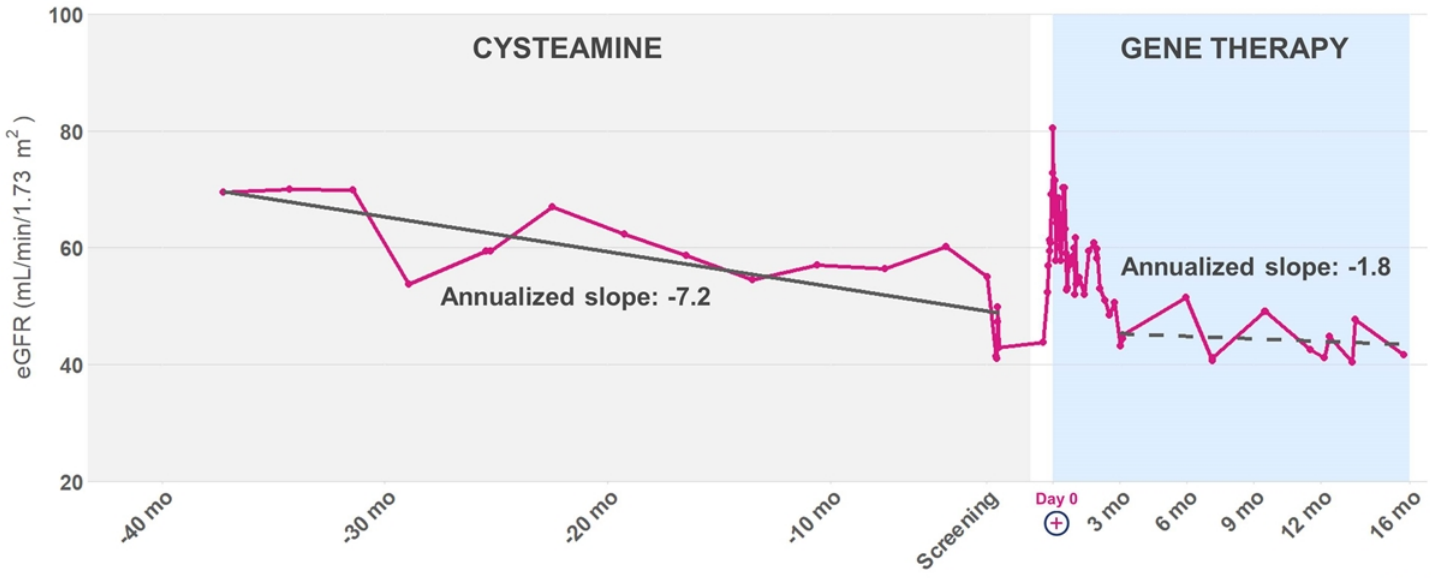
All patients continue to be cysteamine-independent

CYSTINOSIS	PATIENT	MONTHS OFF CYSTEAMINE PILLS AND EYE DROPS POST AVR-RD-04 INFUSION
OFF cysteamine pills	PATIENT 1	16
	PATIENT 2	6
	PATIENT 3	2
OFF cysteamine eye drops	PATIENT 1	16
	PATIENT 2	5
	PATIENT 3	1

Note: All 3 subjects remain off cysteamine pills and eye drops.
Subjects 2 and 3 stopped cysteamine eye drops 1-month post-transplant (per protocol).
Subject 1 stopped cysteamine eye drops prior to baseline.
Data as of January 20, 2021

CYSTINOSIS PHASE 1/2: PATIENT 1

eGFR data at 16 months suggest renal function stabilization post-gene therapy after years of pathological decline

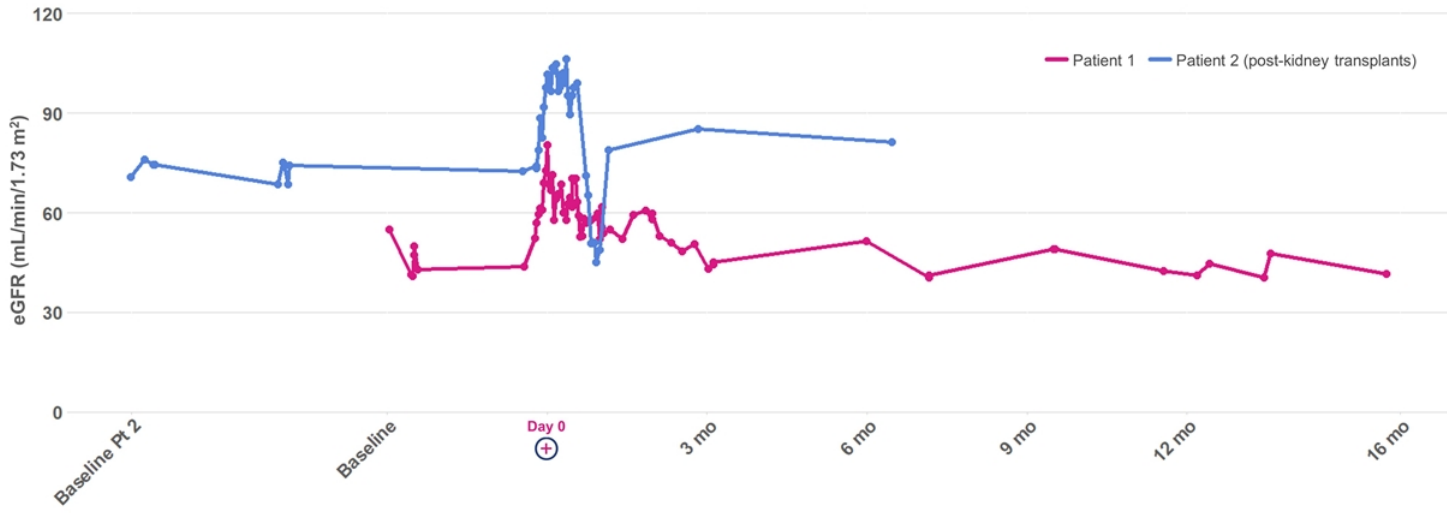


Note: These results are for a single patient only and may vary in the study population; eGFR calculated using CKD-EPI formula; eGFR: Estimated Glomerular Filtration Rate; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

AVROBIO (plato) POWERED BY

Trial designed to demonstrate broad applicability across cystinosis patient population

Positive eGFR trends independent of kidney transplant status



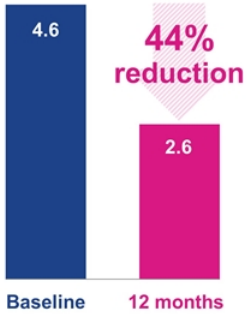
Note: eGFR calculated using CKD-EPI formula
Patient 2 is post two kidney transplants
eGFR: Estimated Glomerular Filtration Rate; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

CYSTINOSIS PHASE 1/2: PATIENT 1

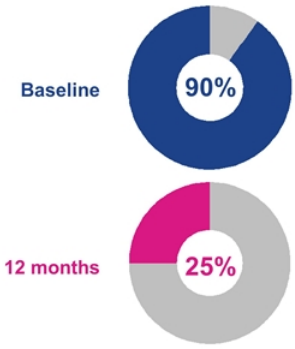
Sharp drop in the number and size of cystine crystals in skin and rectal biopsies

SKIN BIOPSY

Average intracytoplasmic crystals per cell

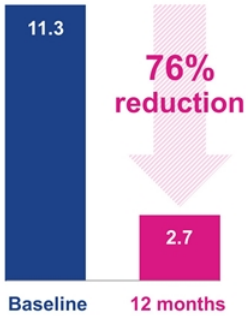


Occupancy of cytoplasmic volume

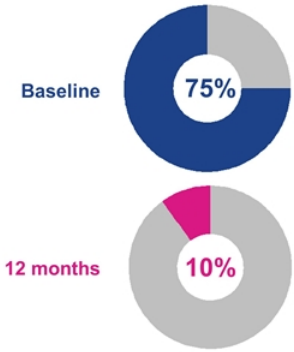


RECTAL BIOPSY

Average intracytoplasmic crystals per cell



Occupancy of cytoplasmic volume



Note: These results are for a single patient only and may vary in the study population

AVROBIO plato

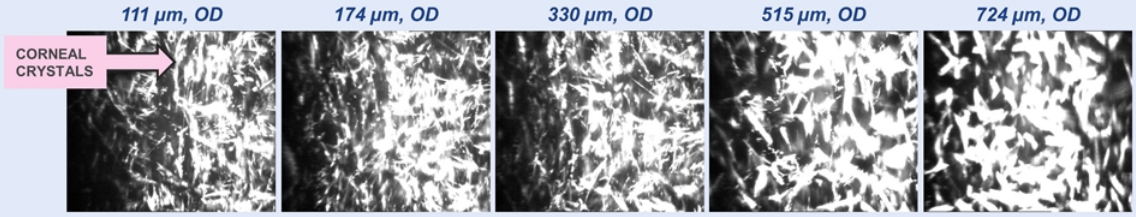
CYSTINOSIS PHASE 1/2: PATIENT 1

Substantial decline in corneal crystals observed at 1 year

***Front** of cornea* — ***Back** of cornea*

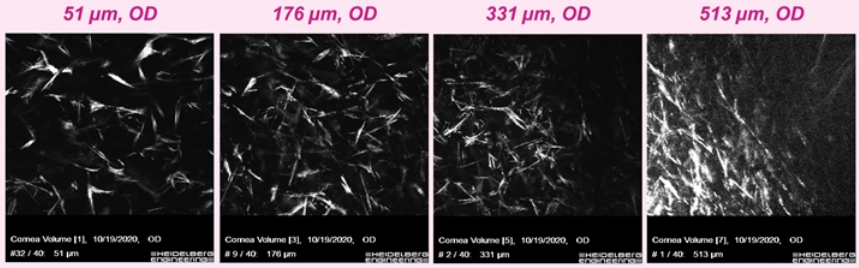
Baseline

IVCM images from Nidek Confoscan



12 months post-gene therapy

IVCM images from Heidelberg HRT3 w/ Rostock Corneal Module



Note: These results are for a single patient only and may vary in the study population; IVCM: In Vivo Confocal Microscopy; OD: Oculus Dexter (right eye); HRT3: Heidelberg Retina Tomograph 3

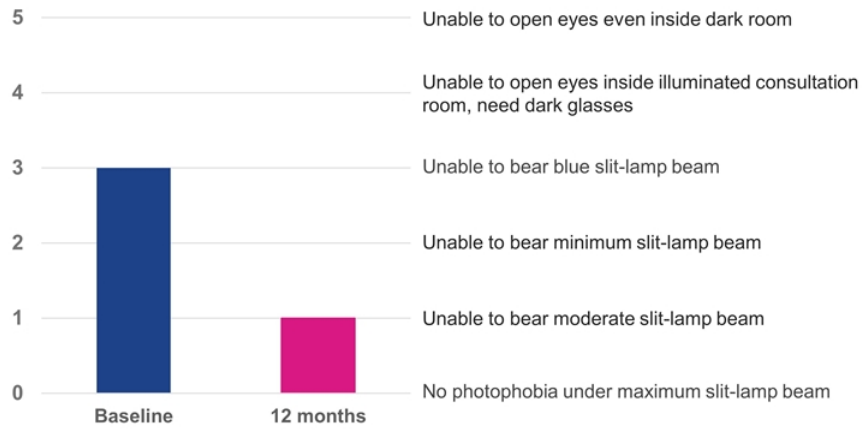
Photophobia improved meaningfully at 1 year

Photophobia, or extreme sensitivity to light, is a hallmark of cystinosis

Cystinosis photophobia intensity associated with:

- Crystal density (light scattering)
- Inflammatory cell infiltration
- Corneal nerve damage

Clinician-Assessed Photophobia Grade
(Patient 1)



Liang, H. IONS May 2015

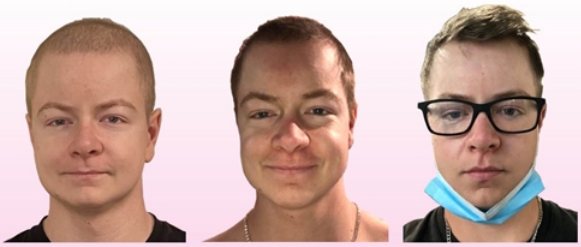
Darker pigmentation may be a sign of multi-functional cystinosin activity post-gene therapy

Cystinosin is located in melanosomes and regulates melanin synthesis

Patient 1 appears to exhibit **progressively darkening skin, eyebrows and hair color post-infusion**, suggesting a possible impact of cystinosin protein on melanin

Blond hair and pale skin typical for cystinosis patients

Pre-Infusion



4 months *6 months* *9 months*

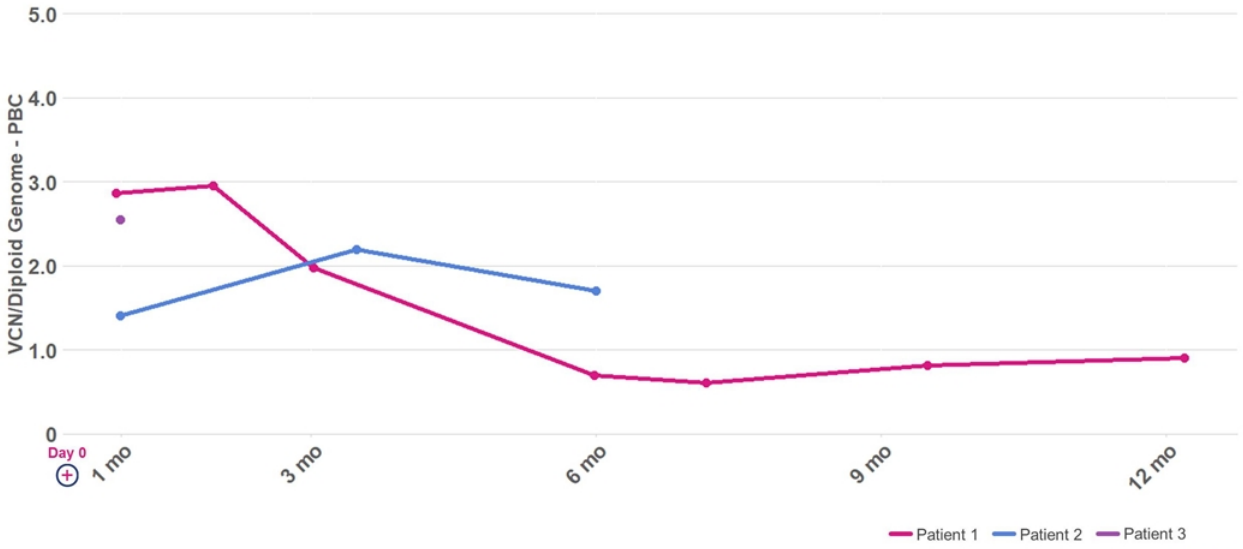
Post-Infusion

Note: These results are for a single patient only and may vary in the study population; Background removed for clarity
Source: Chiaverini et al., FESEB, 2012

VCN trending as expected across patients

Patient 1 reached VCN therapeutic plateau

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

No unexpected safety events

Conditioning-related side effects have been manageable and transient

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

AEs & SAEs reported

- AEs (n=48)
  - Majority of AEs are mild or moderate and resolved
- SAE (n=1)
  - Post AVR-RD-04 treatment: appendicitis unrelated to study treatment or procedures

- AEs are generally consistent with myeloablative conditioning or underlying disease:

Pre-AVR-RD-04 treatment and prior to conditioning (not all events listed)
- Diarrhea, hypokalemia, dizziness
- Dehydration, vomiting

Post-AVR-RD-04 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

Note: Safety database cut as of January 27, 2021
AE: Adverse Event; SAE: Serious Adverse Event

Planned global regulatory strategy for cystinosis

Planned

POTENTIAL REGISTRATION

- Adults and pediatrics, males and females
- Mutation-independent, kidney transplant-independent
- Efficacy, durability, safety
- Ophthalmology, kidney, and other undisclosed
- Multiple crystal measures
- Quality of life

50% Enrolled

PHASE 1/2 – INVESTIGATOR SPONSORED TRIAL

- n ≤6
- Adults and adolescents, males and females
- Mutation-independent, kidney transplant-independent
- Safety, durability, preliminary efficacy
- Biomarker data, kidney function, vision
- Quality of life

Anticipated Next Steps:

- Engage with FDA on registration trial design
- Identify global sites for registration trial
- Prepare plato® CMC / analytics requirements

FDA: Food and Drug Administration; CMC: Chemistry, Manufacturing, and Controls

Gaucher disease type 1 opportunity

Adrianna, living with Gaucher disease type 1

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*

Unmet needs with SOC:

Bone-related manifestations
Skeletal abnormalities, avascular necrosis, osteoporosis

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

Hepatosplenomegaly
Enlarged liver, enlarged spleen

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

CNS complications
Increased risk of GBA-Parkinson's disease

Gaucher Disease Type 1 Target Product Profile**:

- Prevents, halts or reverses disease; extends/normalizes lifespan
- Addresses all patient segments – all GD1 genetic mutations, all ages, male & female
- Lifelong durability – single infusion; off ERT/chaperone therapy
- Impacts hard-to-reach organs – e.g., brain, bone and bone marrow
- Well tolerated

Affects ~ 1:44,000 people worldwide

** WAC pricing from Redbook using standard dosing assumptions*
*** Note: these are target attributes for a first-line therapy*

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

PHASE 1/2
AVR-RD-02

An **adaptive, 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:

RECRUITING PLANNED 2021:

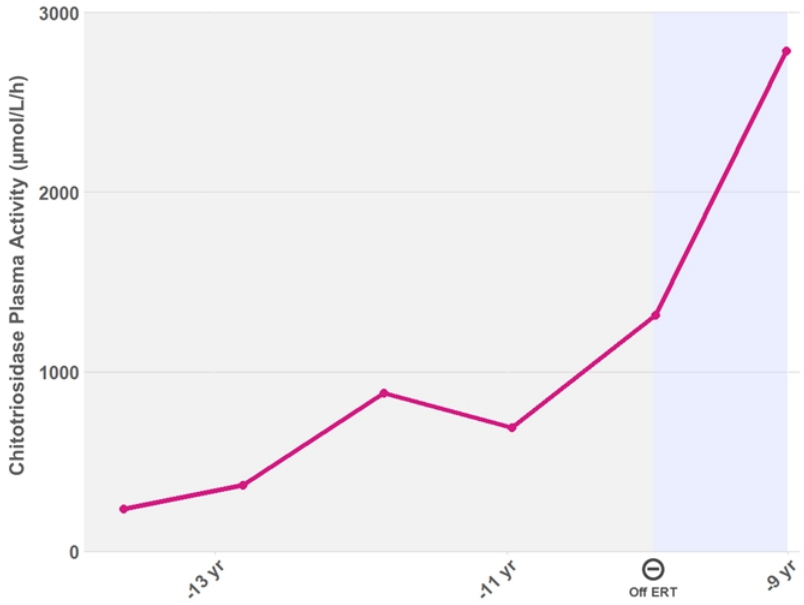
OBJECTIVES	PATIENTS	
• Safety • Efficacy • Engraftment	• Enrollment goal 8-16 patients • 18-45-year-old males and females • Have a confirmed diagnosis of GD1 based on: – Deficient glucocerebrosidase enzyme activity – Clinical features consistent with GD1	**Gaucher disease type 1 patients who are:** • ERT-stable for >24 months *or* • Treatment-naïve *or* • Have not received ERT or SRT in the last 12 months

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)

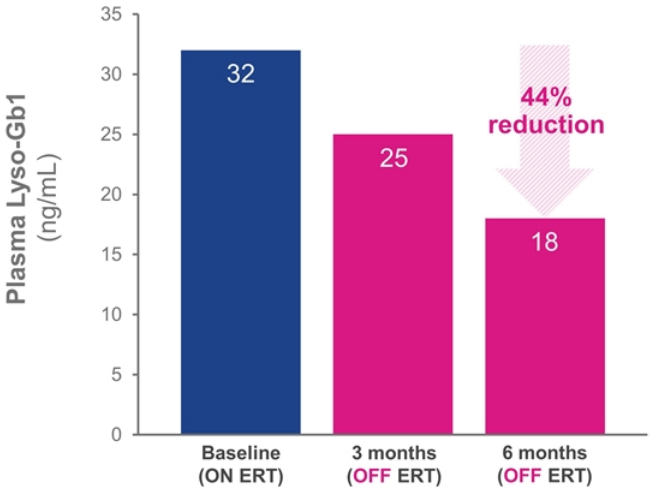


Chitotriosidase Plasma Activity Normal Range: 0.0–44.2 µmoL/L/h
ERT: Enzyme Replacement Therapy

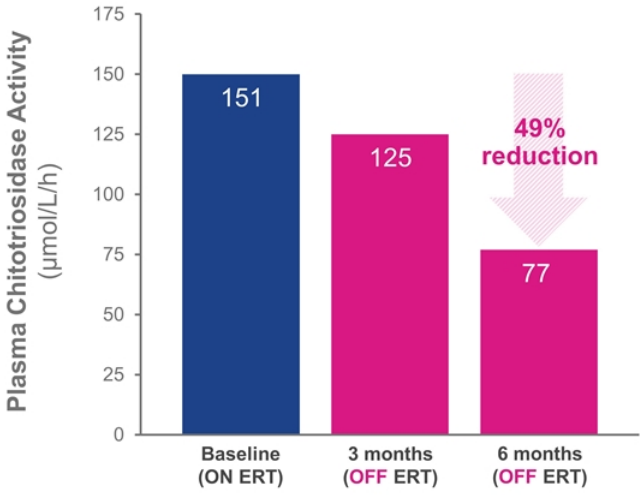
GUARD1: PATIENT 1

Key biomarkers below ERT baseline at 6 months

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



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

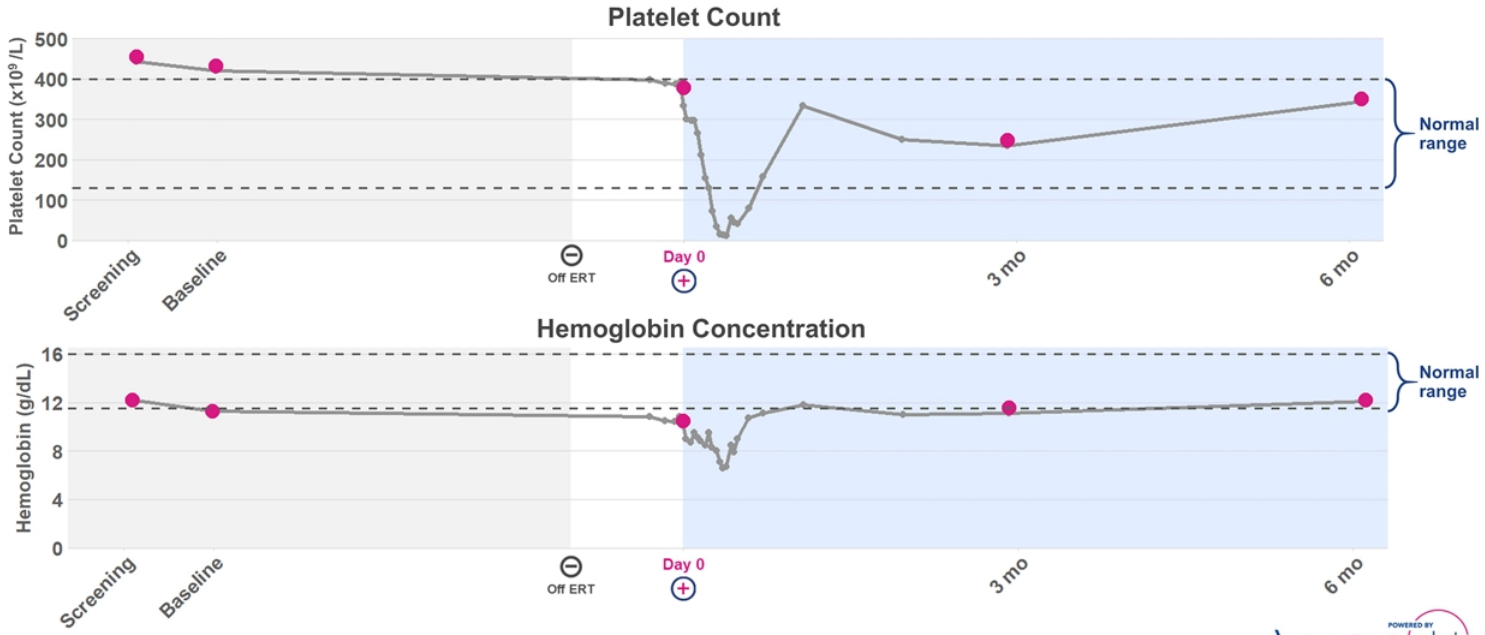


Baseline taken one month prior to gene therapy which is when ERT is discontinued
Lyso-Gb1 Plasma Normal Range: 0.5 – 1.2 ng/mL
Plasma chitotriosidase activity normal range: 0.0 – 44.2 µmoL/L/h
ERT: Enzyme Replacement Therapy

AVROBIO powered by plato

GUARD1: PATIENT 1

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



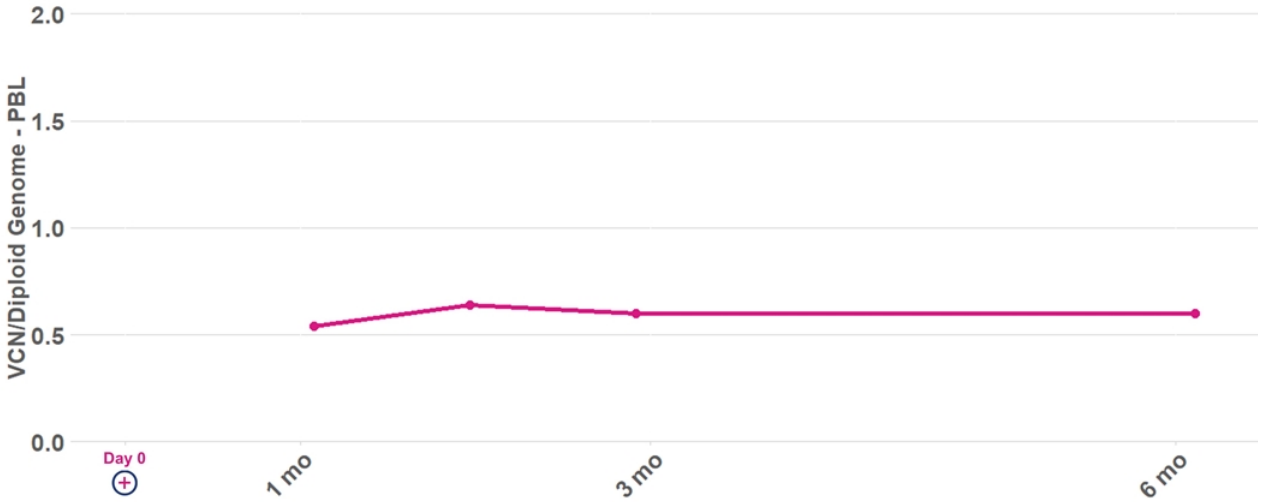
Platelet Count Reference Value Adult: 130-400x109/L; Hemoglobin Reference Value: Males: 13.5-17.5 g/dL; Females: 11.5-16.0 g/dL; grey line: local (safety) lab values; pink dots: central (efficacy) lab values; ERT: Enzyme Replacement Therapy

AVROBIO powered by plato

GUARD1: PATIENT 1

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

GUARD1: PATIENT 1

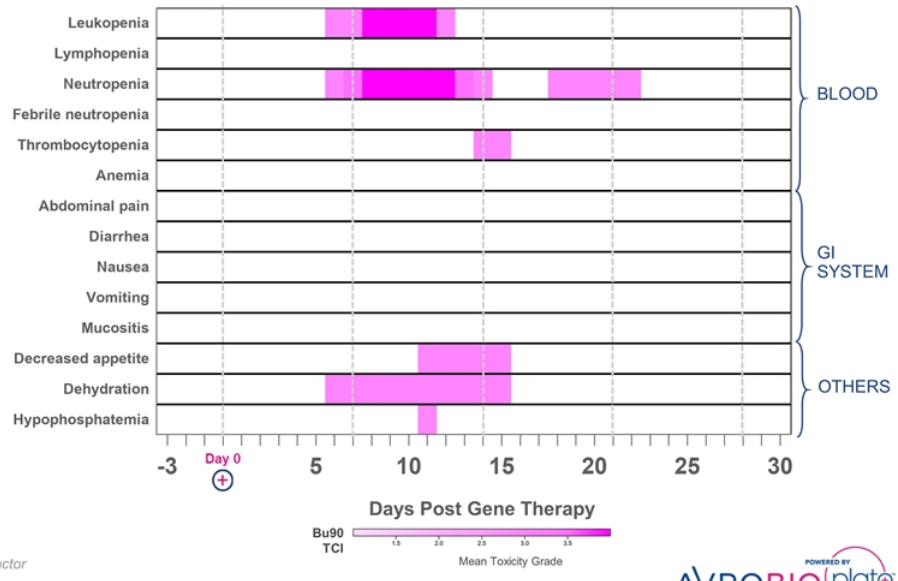
No unexpected safety events identified in first patient

Conditioning-related side effects have been predictable and transient

AEs (no SAEs reported)

- No AEs or SAEs related to AVR-RD-02 drug product
- AEs generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
- AEs n=29
  - Grade 3 (n=7)
    - Eye pain, decreased appetite, dehydration, headache, hypophosphatemia, neutropenia, thrombocytopenia
  - Grade 4 (n=2)
    - Leukopenia and neutropenia
- AEs resolved without clinical sequelae

Conditioning-related grade 3/4 AEs



Note: Safety database cut as of January 04, 2021
AE: Adverse Event; SAE: Serious Adverse Event; G-CSF: Granulocyte Colony Stimulating Factor
G-CSF 5 µg/kg @ Days 5, 6, 7, 10, 11, and 14 post-infusion of AVR-RD-02
Bu90-TCI: Busulfan 90-Target Concentration Intervention; GI: Gastrointestinal

Planned global development strategy for Gaucher disease type 1

Planned

POTENTIAL REGISTRATION PATH

- Phase 1/2 expansion
- Safety, efficacy, durability
- Organ volumes, hematologic measures, bone assessments, pain, and QOL

Enrolling

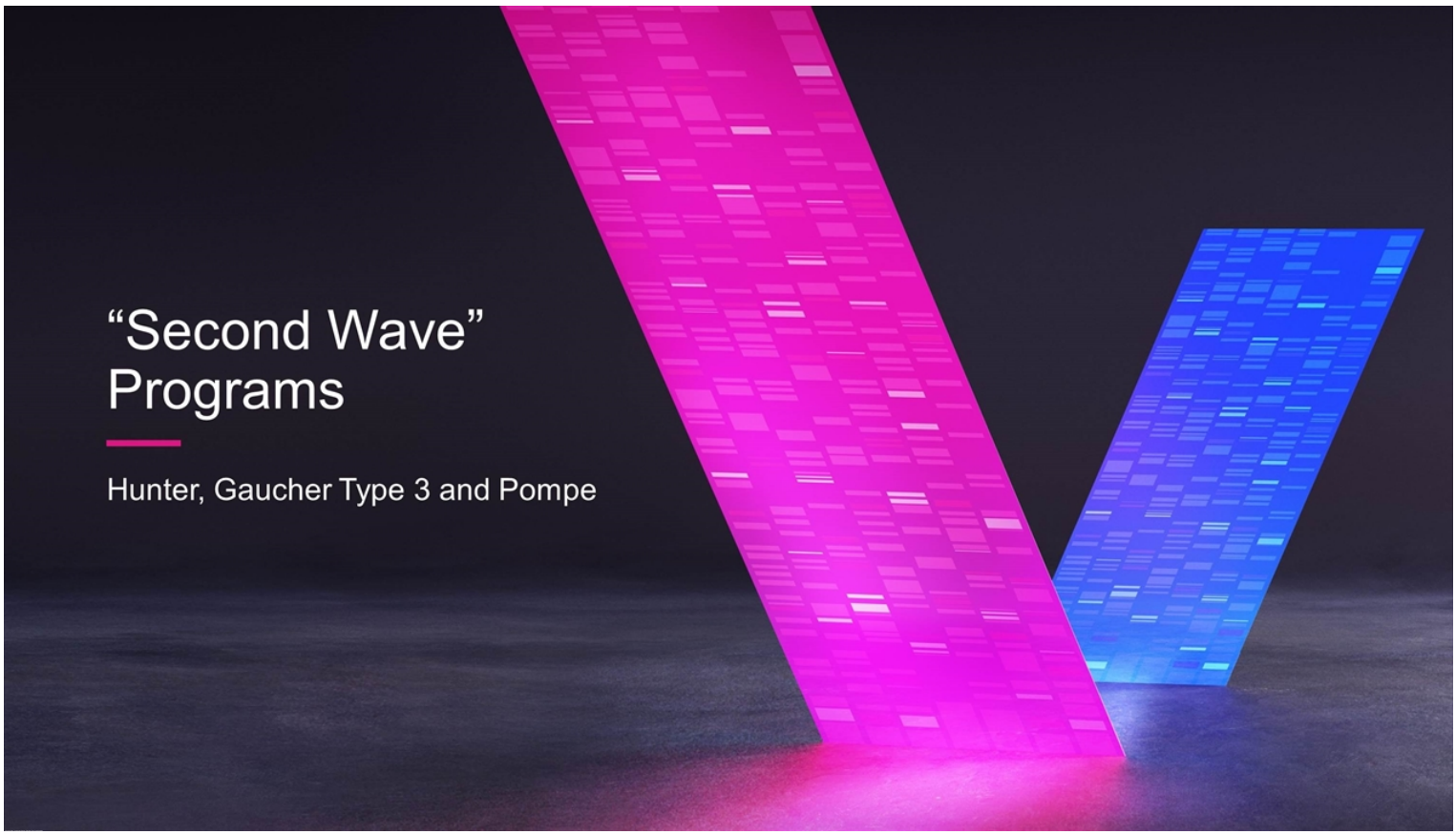
PHASE 1/2

- n=8-16
- Adults, males and females, ages 18-45 years old
- ERT-switch and ERT-naïve
- Safety, efficacy, durability
- Biomarker data, organ volumes, hematologic measures, bone assessments, pain, and QOL

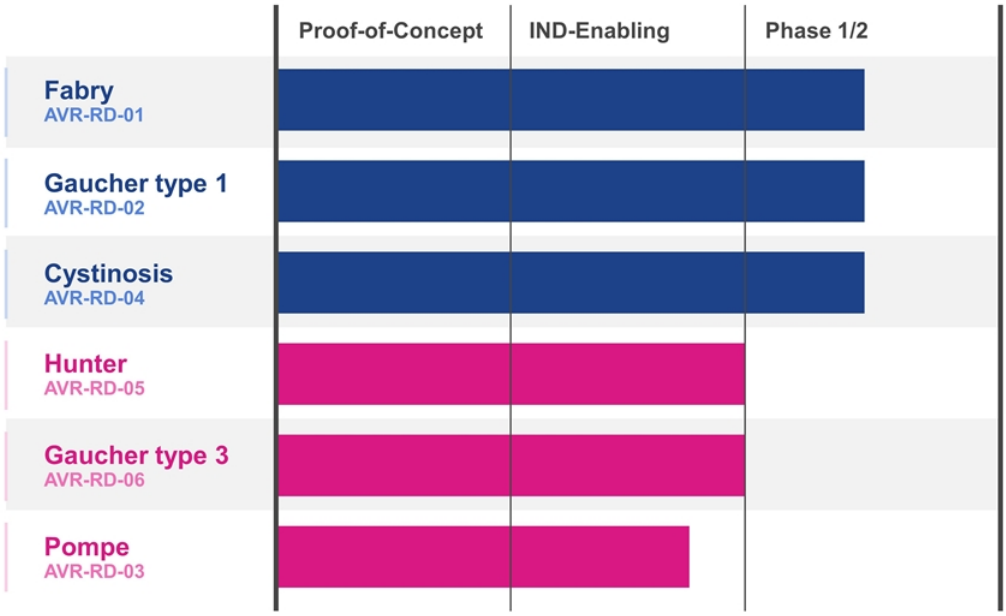
Anticipated Next Steps:

- Advance patient enrollment
- Advance regulatory dialogue on registration pathway

QOL: Quality Of Life; ERT: Enzyme Replacement Therapy


“Second Wave”
Programs
Hunter, Gaucher Type 3 and Pompe

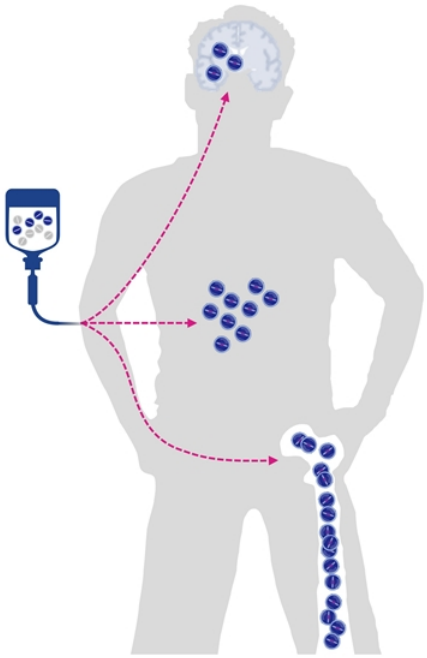
Bold expansion of our leadership in lysosomal disorders

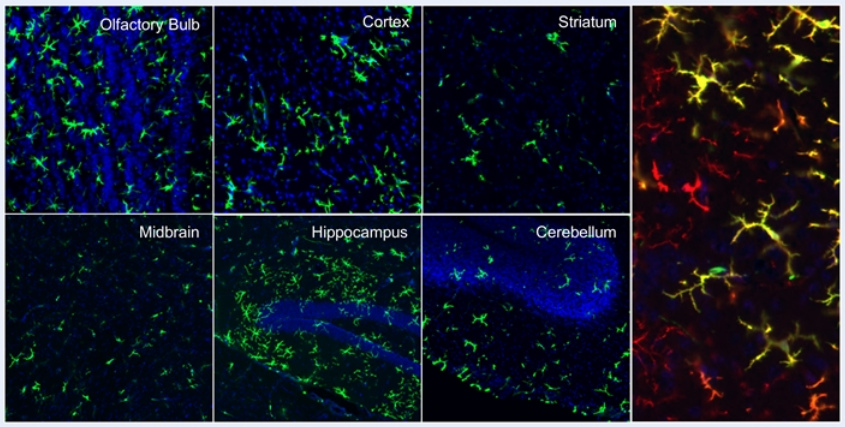


IND: Investigational New Drug

PRECLINICAL DATA

Lentiviral gene therapy enables global distribution of functional enzyme to brain and bone in preclinical studies





GFP: Green Fluorescent Protein; DAPI: 4',6-diamidino-2-phenylindole; Iba1: Ionized Calcium-Binding Adapter Molecule 1; IV: Intravenous

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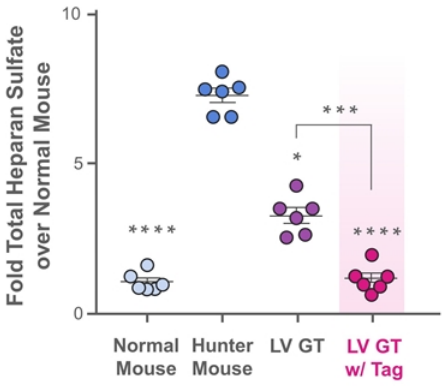
Proprietary tags deliver therapeutic protein into hard-to-reach organs

Hunter syndrome

Tag normalizes heparan sulfate in brain



Pompe disease

Tag normalizes glycogen substrate in brain

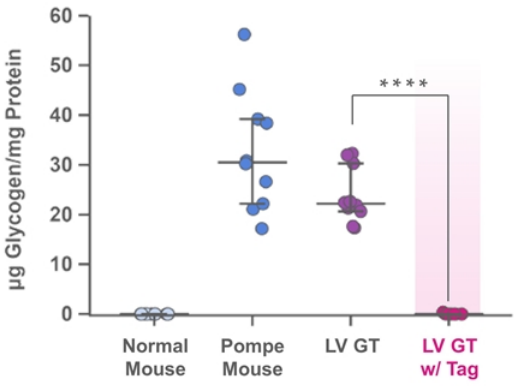


*Figure adapted from Gleitz H et al., EMBO Mol Med, 2018 Fig 3A; *P<0.05, ***P<0.001, ****P<0.0001; LV GT: Lentiviral Gene Therapy*

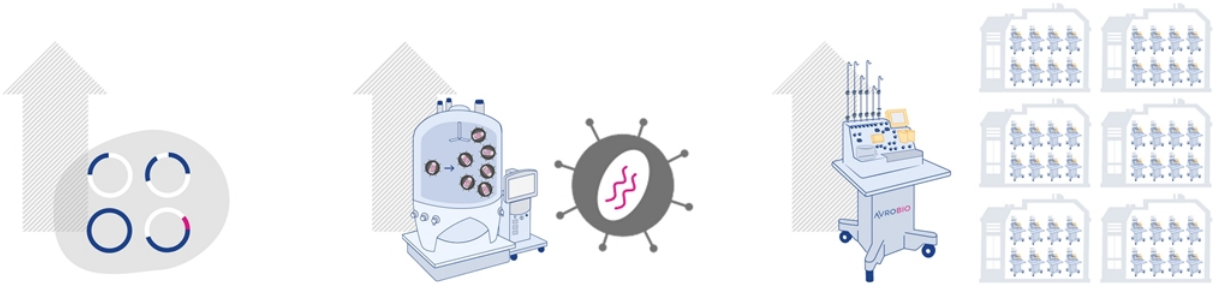
plato®

AVROBIO's platform for global gene therapy commercialization

- Redefines manufacturing best practices
- Solves key industry challenges

Designed to be fully scalable

Common components and automation leveraged across manufacturing



PLASMID

3 of 4 component plasmids used in every vector

Each plasmid can be mass produced and stored for use

VECTOR

State of the art, largest scale, 200L vector production

Expansion through simple installation of additional units, mass produced, frozen, and stored for use

DRUG PRODUCT

Closed system automated platform

Scale out of manufacturing suites and automation units to meet patient demand

Note: This diagram is for illustrative purposes only

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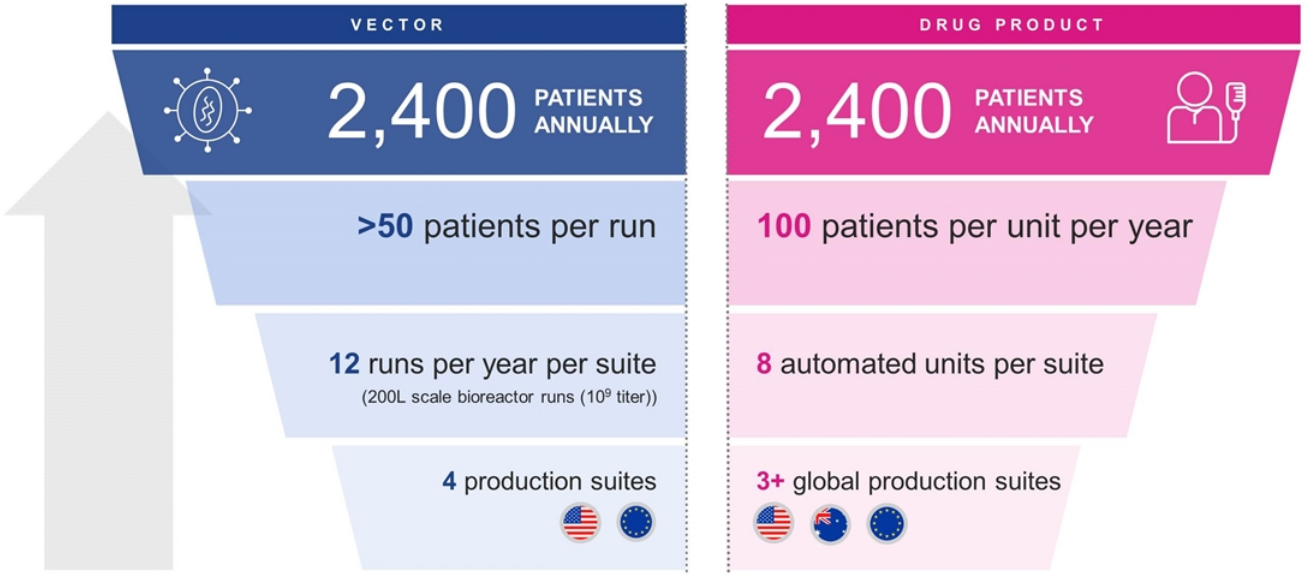
Poised to manufacture at scale

Global infrastructure already in place



Note: This diagram is for illustrative purposes only

CMC achievements have defined the plato® story

Strategic investment in technology laid the foundation for our manufacturing leadership

Manufacturing

Robust production platform

- Best-in-class LV manufacturing
- Scalable from plasmid to drug product

Global footprint

- In the clinic in multiple jurisdictions

Cost effective

- Intended to address key COGs issues

Analytics

Robust platform analytics

- Best-in-class VCN assay
- First-in-class transduction assay

Deep product characterization

- First-in-class single cell analytics

Potency assay matrix

- Intended to accelerate regulatory approvals

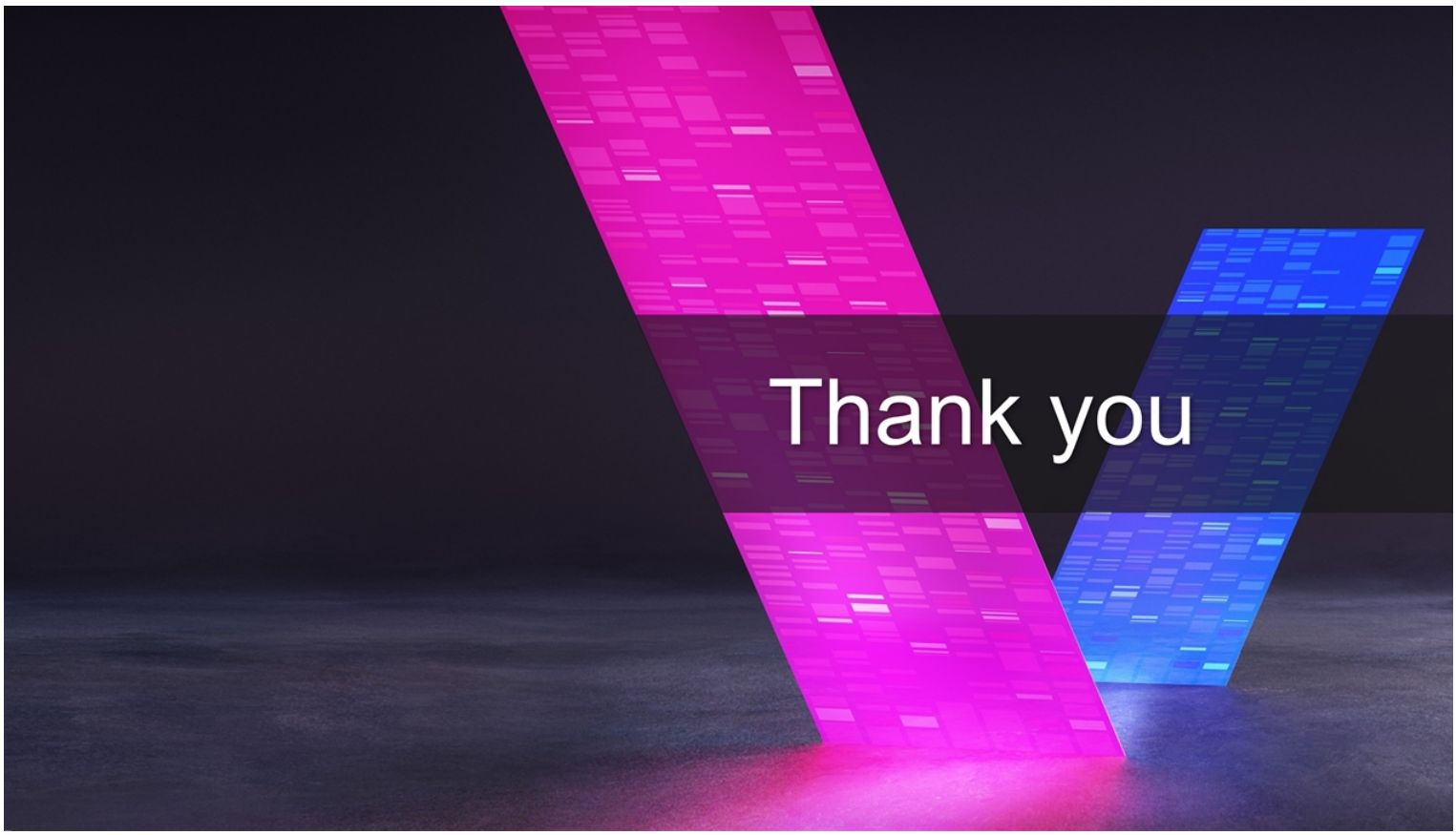
CMC: Chemistry, Manufacturing, and Controls; VCN: Vector Copy Number; LV: Lentiviral; COGs: Cost Of Goods

Key anticipated 2021 milestones

Goal: 30 patients dosed cumulatively by end of 2021

Fabry AVR-RD-01	Seek agreement with regulators on approval pathway in one or more major markets
Gaucher type 1 AVR-RD-02	Execute on global phase 1/2 trial
Cystinosis AVR-RD-04	Engage w/ FDA on pivotal trial design
Hunter AVR-RD-05	Conduct Phase 1/2 trial initiation activities
Gaucher type 3 AVR-RD-06	FDA dialogue on path to clinic
Pompe AVR-RD-03	Prepare for classic infantile-onset study

FDA: Food and Drug Administration


Thank you

Appendix

Fabry Phase 1 & 2 Patient Characteristics

	PHASE 1: ERT-Treated Fabry Patients				
	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4	PATIENT 5
Age of symptom onset / diagnosis	18 / 37 years	9 / 29 years	10 / 0 years	7 / 4 years	10 / 14 years
Years on ERT	11 years	6 years	4 years	11 years	2 years
Age dosed with AVR-RD-01	48 years	39 years	40 years	37 years	30 years
Mutation	c.962A>G (p.Q321R)	c.1033T>C (p.S345P)	c.427G>C (p.A143P)	c.427G>C (p.A143P)	(p.Y134S)
Leukocyte AGA activity at baseline (nmol/hr/mg protein)**	2.1	1.1	0.6	2.2	1.0
Plasma lyso-Gb3 at baseline (nM)***	25	26	59	29	16
eGFR (mL/min/1.73m^2) at baseline**	83	49	112	124	121
ERT discontinuation status	18 months after gene therapy dose		Did not resume ERT after gene therapy dose	6 months after gene therapy dose	

	PHASE 2: Treatment-naïve Fabry patients			
	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4
Age of symptom onset/diagnosis	10 / 19 years	36 / 37 years	13 / 13 years	9 / 9 years
Age dosed with AVR-RD-01	21 years	46 years	40 years	26 years
Mutation	c.1021G>A (p.E341K)	c.644A>G (p.N215S)	c.639+1G>T	c.833dupA
Leukocyte AGA enzyme activity at baseline (nmol/hr/mg protein)	0.10*	2.38**	0.58**	0.46**
Plasma lyso-Gb3 at baseline (nM)***	202	8	147	92
eGFR (mL/min/1.73m^2) at baseline**	128	106	98	129
Comment	Few IgA deposits in kidney biopsy, no mesangial proliferation	Cardiac variant, not a classic Fabry male		

** Mayo Lab, ref range ≥23.1 nmol/hr/mg protein; ** Rupar Lab, ref range 24-56 nmol/hr/mg protein; *** Reference value ≤ 2.4 nM; **** eGFR: Estimated Glomerular Filtration Rate; calculated using CKD-EPI formula*
AGA: α-galactosidase A; Lyso-Gb3: Globotriaosylsphingosine;

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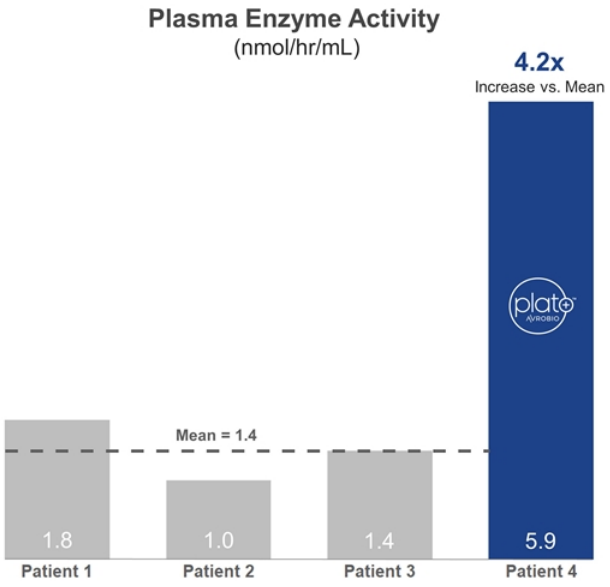
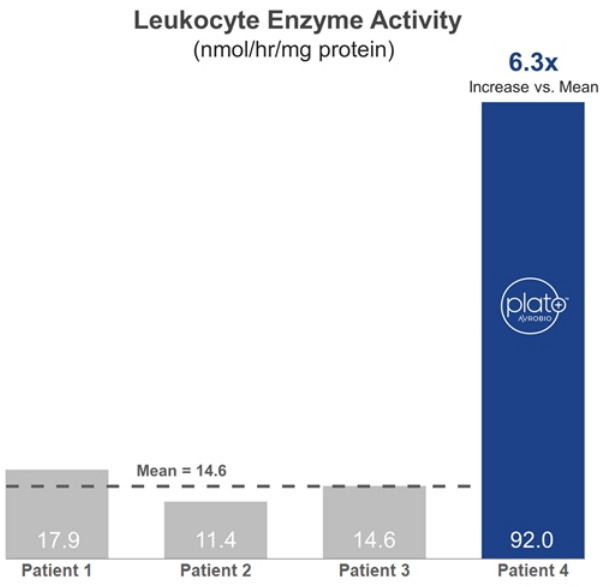
Patient #4 is first Fabry patient dosed with plato®

FAB-GT 12 month data for patient #4 with plato® vs. patients #1-3





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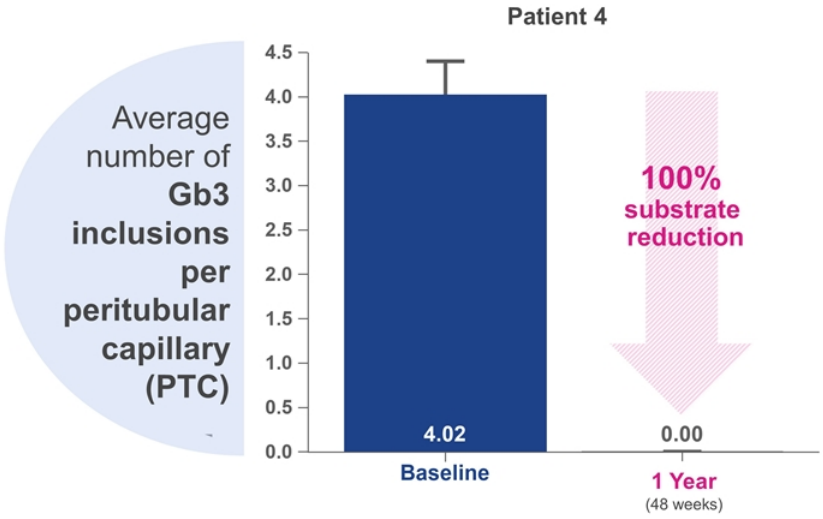
100% clearance of substrate in kidney biopsy at 1 year

Patient dosed using plato®

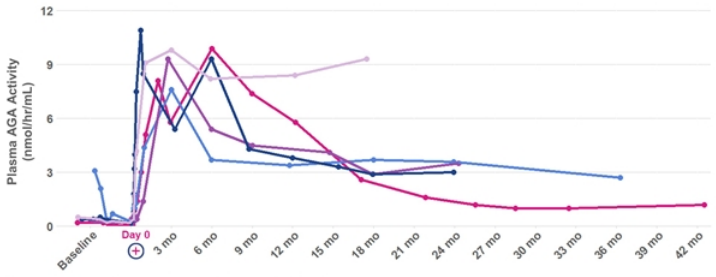


- *Two-sample t-test for difference between average PTCs at Baseline vs. 48 weeks; $p < 0.0001$; Error bar represents the standard error at Baseline (n=103 PTCs) and 48 weeks (n=99 PTCs); scored by 2 independent, blinded pathologists*

Baseline: The last available, non-missing observation prior to AVR-RD-01 infusion
Note: With respect to Fabry disease, Gb3 inclusions per PTC is interchangeable with GL-3 inclusions per KIC
PTC: Peritubular Capillary; Gb3: Globotriaosylceramide; GL-3: Globotriaosylceramide; KIC: Kidney Interstitial Capillary

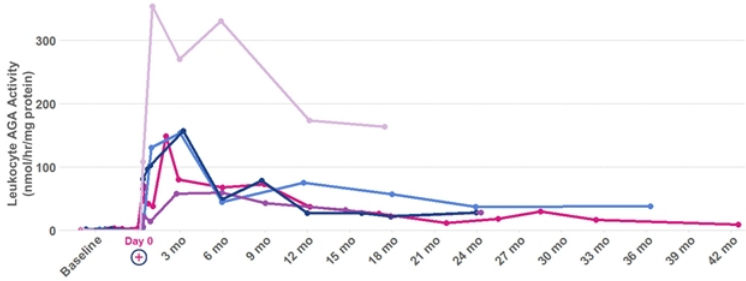
Durability demonstrated over multiple measures up to 3.5 years

Plasma AGA Enzyme Activity



Plasma AGA Activity Reference Range: 5.1–9.2 nmol/hr/mL; AGA: α-galactosidase A

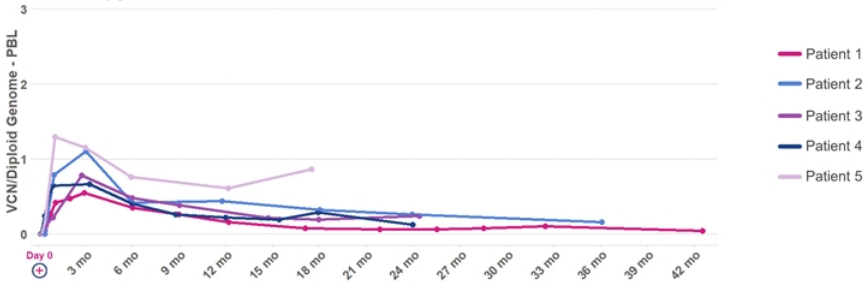
Leukocyte AGA Enzyme Activity



Leukocyte AGA Activity Reference Range: 24–56 nmol/hr/mg protein; AGA: α-galactosidase A

Vector Copy Number

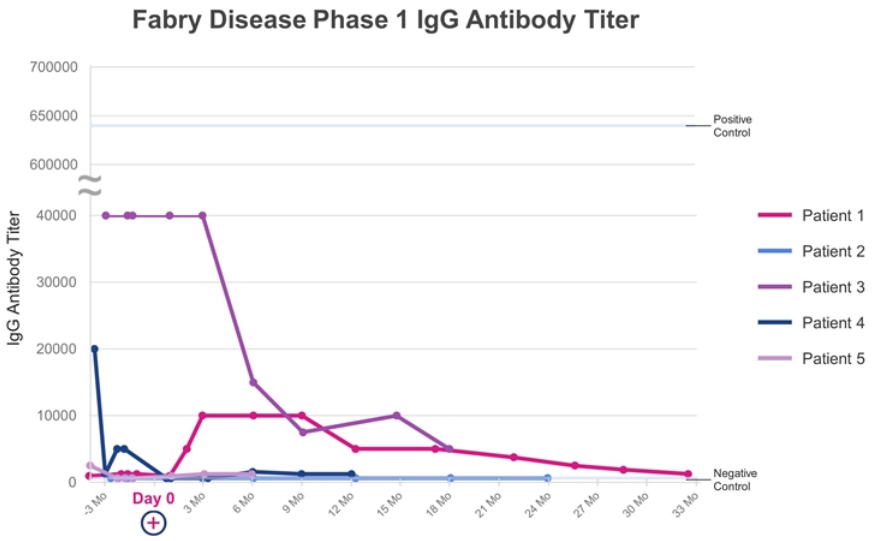
Drug Product VCN/dg
Patient 1: 0.7 **Patient 2: 1.4**
Patient 3: 0.8 **Patient 4: 1.4**
Patient 5: 1.2



VCN: Vector Copy Number; PBL: Peripheral Blood Leukocytes; dg: Diploid Genome

Reduction of pre-existing anti-ERT drug IgG antibodies

Suggests potential as a therapeutic option independent of pre-existing antibodies



Similar results observed in other studies

San Raffaele Telethon Institute for Gene Therapy (SR-TIGET)

Change in pre-existing antibodies reported for Hurler disease (MPS-1)

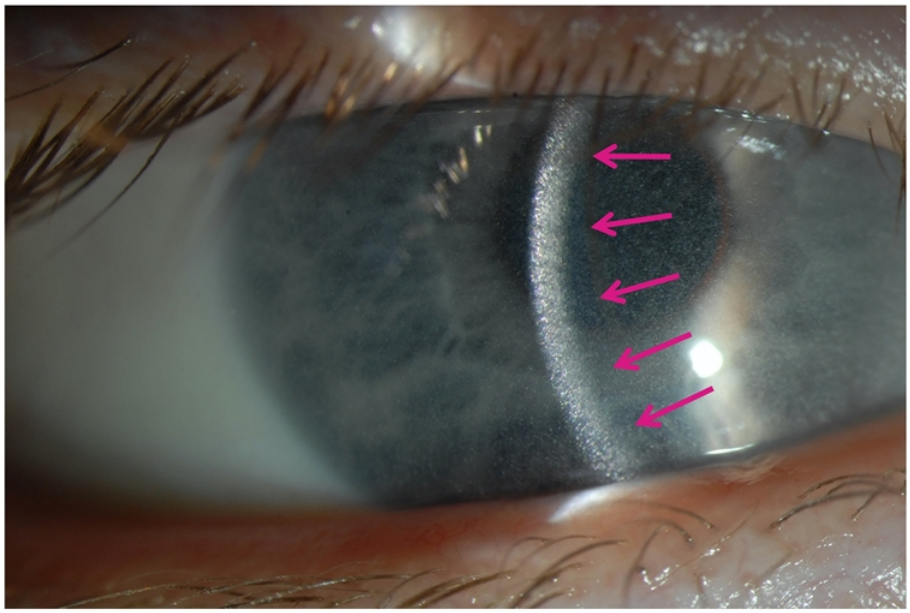
- *Ex vivo* LV gene therapy with conditioning
- n=6
- Evaluable patients (5/6) demonstrated sustained, supraphysiologic blood IDUA activity
- 4/5 prior ERT (rhIDUA) exposure (5-28 months)
- 4/5 pre-existing ERT-induced IgG antibodies
- 6/6 anti-rhIDUA IgGs undetectable 2 months post-gene therapy

Source: Gentner B et al., Blood, 2019

ERT: Enzyme Replacement Therapy; IgG: Immunoglobulin G; MPS-1: Mucopolysaccharidosis Type 1; IDUA: Iduronidase: SR-TIGET: San Raffaele Telethon Institute for Gene Therapy; LV: Lentiviral; rhIDUA: Recombinant Human alpha-L-Iduronidase

Crystal buildup in eye clearly visible before gene therapy

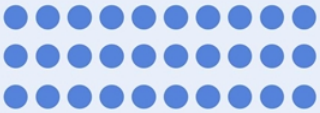
Patient 1 at baseline



Impact of cysteamine independence

Daily cysteamine regimen

(max per day)

	ON cysteamine pills	*ON* cysteamine eye drops
Before AVR-RD-04	**30 pills / day** 	**Prescribed 8 drops / day** 
After AVR-RD-04 (16 months post-gene therapy)	*OFF* cysteamine pills **0 pills / day**	*OFF* cysteamine eye drops **0 drops / day**

Note: These results are for a single patient only and may vary in the study population; does not include supplements and other medications
Data as of January 20, 2021