

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 13, 2020

AVROBIO, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-38537
(Commission
File Number)

81-0710585
(I.R.S. Employer
Identification No.)

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

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

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

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

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

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

Emerging growth company

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

Item 7.01 Regulation FD Disclosure.

On May 13, 2020, AVROBIO, Inc. (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 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 and Exhibit 99.1 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 8.01 Other Events.

On May 13, 2020, the Company issued a press release titled "AVROBIO Reports Updated Clinical Data from Investigational Gene Therapy Programs for Fabry Disease and Cystinosis." A copy of the press release 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. slide presentation, dated May 13, 2020.](#)

99.2 [Press release issued by AVROBIO, Inc., dated May 13, 2020.](#)

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.

Date: May 13, 2020

AVROBIO, INC.

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

AVROBIO

ASGCT 2020
Fabry & Cystinosis Data Update
May 13, 2020



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.

This presentation may contain forward-looking 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, prospective products and goals, the therapeutic potential 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, potential regulatory approvals and the timing thereof, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, the expected benefits and results of our implementation of the plato™ platform in our clinical trials and

gene therapy programs, the expected benefits of Saladax Biomedical's immunoassay kits and Magenta Therapeutics' antibody-drug conjugate (MGTA-117), including, in each case, the potential application to our investigational gene therapies, the expected safety profile of our investigational gene therapies, timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated products. Any such statements in this presentation that are not statements of historical fact may be deemed to be forward-looking statements.

Any forward-looking statements in this presentation 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 investigational gene therapies 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 or of encountering challenges in the enrollment or dosing in such 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 AVROBIO may not realize the intended benefit of Saladax's immunoassay kits and/or Magenta's MGTA-117 with respect to AVROBIO's investigational gene therapies, the risk that our investigational gene therapies 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 investigational gene therapies, the risk that we will be unable to obtain and maintain regulatory approvals for our investigational gene therapies, the risk that the size and growth potential of the market for our investigational gene therapies 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 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 investigational gene therapies. 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 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.

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



ASGCT 2020 data update – key takeaways



New data show consistent results across Fabry disease and cystinosis programs

Long-term Fabry patient data

Sustained long-term positive trends

- Patient 1 in the Phase 2 trial continues to show stable leukocyte and plasma AGA enzyme activity, now out 22 months
- Patient 3 in the Phase 2 trial shows increased leukocyte and plasma AGA enzyme activity, decreased plasma lyso-Gb3 level, and stable VCN at new time points
- All three Phase 1 patients off ERT remain off ERT

First Fabry plato™ patient

plato continues to perform

- One-month plasma lyso-Gb3 decrease of 43% vs. baseline
- Three-month leukocyte and plasma enzyme activity levels 3x greater than mean of other three patients at same timepoint in Phase 2 trial
- Rapid neutrophil and platelet recovery with minimal lymphocyte depletion post Bu90 conditioning

Cystinosis Patient 1 data

Positive trends at six months, including kidney function measures

- eGFR and serum creatinine measures trending positively at 6 months
- Pill burden remains significantly lower than at baseline



Multiple programs in the clinic

10 patients dosed to date

Investigational Gene Therapy	Proof-of-Concept	IND-Enabling	Phase 1/2	Commercial Rights
Fabry AVR-RD-01 	Phase 2			AVROBIO
Gaucher AVR-RD-02 	Phase 1/2			AVROBIO
Cystinosis AVR-RD-04 	Phase 1/2			AVROBIO
Pompe AVR-RD-03 	Preclinical			AVROBIO

IND: Investigational New Drug



Fabry Disease



AVR-RD-01



Goals for gene therapy in Fabry disease

UNMET NEEDS:



Kidney function

Unmet needs: proteinuria, polyuria, kidney failure



Cardiac function

Unmet needs: left ventricular hypertrophy, fibrosis, heart failure



Neuropathic pain

Unmet needs: pain and burning sensations in hands and feet, pain crises



CNS complications

Unmet needs: TIA/stroke, depression, impaired executive function, white matter hyperintensities



Everyday burden of illness and life expectancy

Unmet needs: fatigue, inability to sweat, joint pain, abdominal pain, diarrhea, vomiting, cloudy vision, hearing loss, tinnitus, rash, angiokeratomas, biweekly infusions, shortened lifespan



Two AVR-RD-01 Fabry clinical trials

9 patients dosed across Phases 1 and 2



PHASE 1

Investigator-Sponsored Trial*

Patients

n = 5 (fully enrolled)
On ERT > 6 months prior to enrollment
18-50 year-old males

Key Objective

Safety and preliminary efficacy

PHASE 2

AVRO – FAB-201 Trial

Patients

n = 8-12 (4 patients dosed to-date)
Treatment-naive
16-50 year-old males

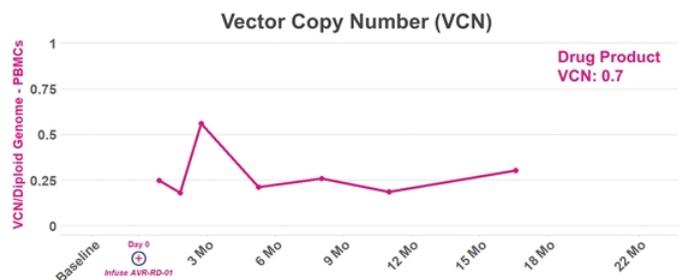
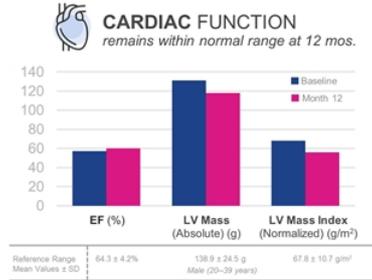
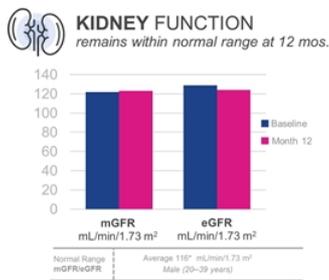
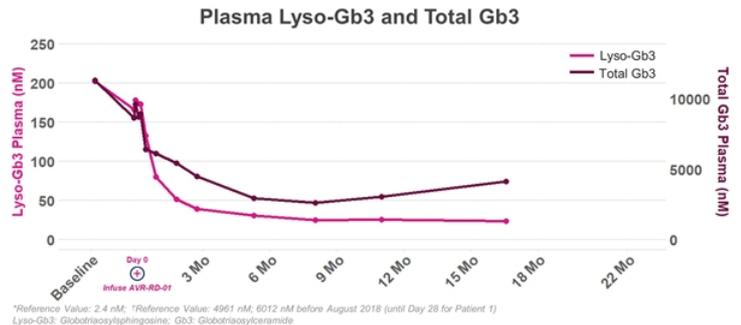
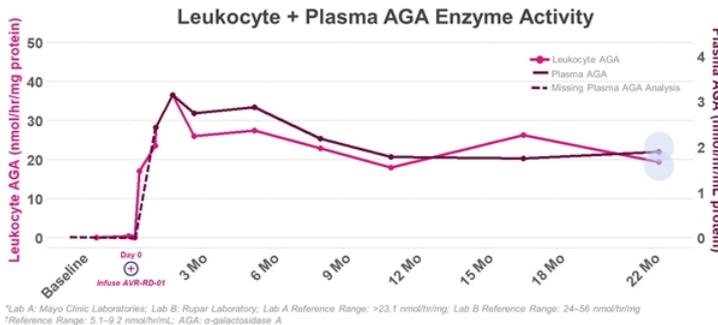
Key Objectives

Safety and efficacy

* Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada



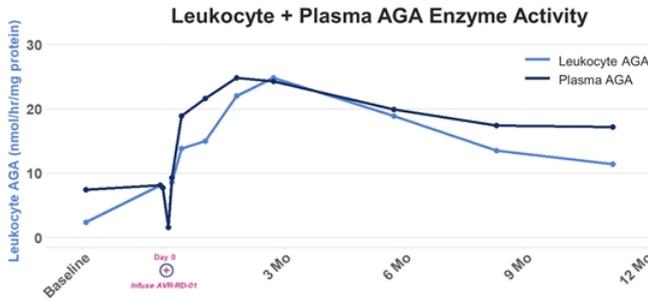
Patient 1: Multiple data trends sustained up to 22 months



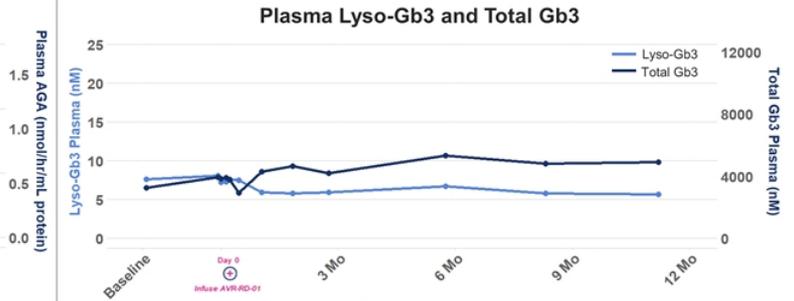
Note: Patient #1 had a skin biopsy score of 3 (severe accumulation) at baseline, a score of 2 (moderate accumulation) at 6 months and a score of 1 (mild accumulation) at 12 months
Note: Visualization of multiple biomarkers adjusted to utilize the same statistical scaling ratio across biomarkers (as compared to prior presentation)



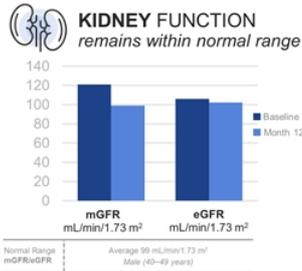
Patient 2: Multiple data trends sustained up to 1 year*



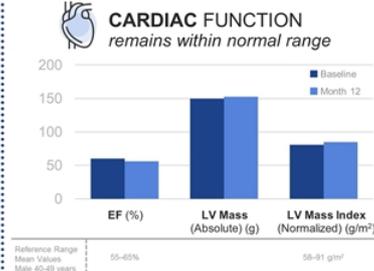
*Data from Rupa Laboratory; Reference Range: 24–56 nmol/hr/mg; †Reference Range: 5.1–9.2 nmol/hr/mL; AGA: α-galactosidase A



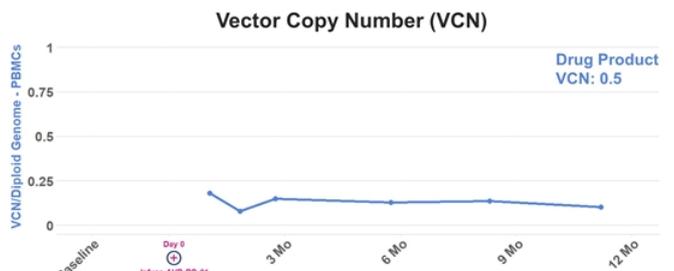
*Reference Value: 2.4 nM; †Reference Value: 4961 nM; Note: Patient #2 has normal substrate, consistent with late-onset cardiac variant phenotype
Lyso-Gb3: Globotriaosylsphingosine; Gb3: Globotriaosylceramide



Source: <https://www.kidney.org/atoz/content/gfr>
mGFR: Measured Glomerular Filtration Rate; eGFR: Estimated Glomerular Filtration Rate



Source: Alfakih K et al. J Magn Reson Imaging. 2003
EF: Ejection Fraction; LV: Left Ventricular



VCN: Vector Copy Number; PBMCs: Peripheral Blood Mononuclear Cells

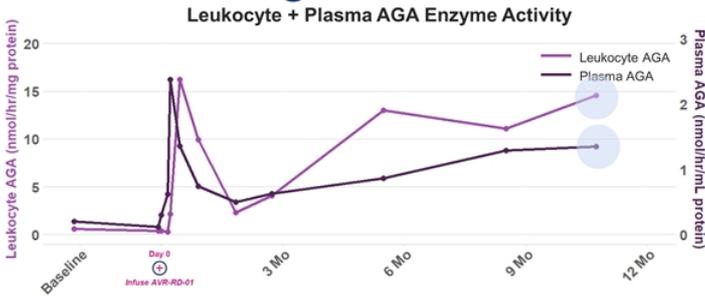
Note: As patient #2 is a cardiac variant of Fabry disease, this patient had a skin biopsy score of 0 (trace or no accumulation) at baseline and at 6 months

Note: Visualization of multiple biomarkers adjusted to utilize the same statistical scaling ratio across biomarkers (as compared to prior presentation)

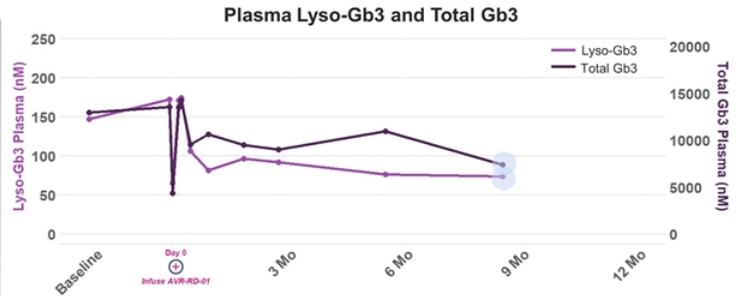
* Latest data points for this patient are at the 1-year follow-up which = 48 weeks per protocol



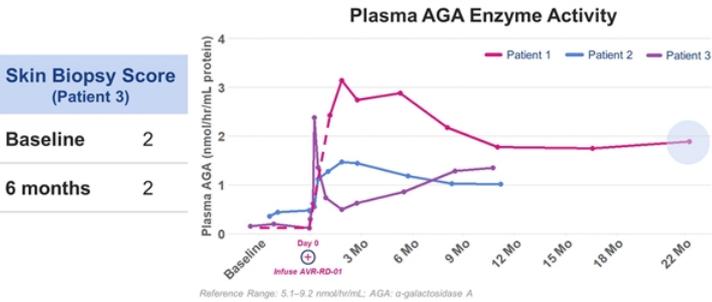
Patient 3: Data up to 1 year* suggest trend towards durable engraftment



*Data from Ripar Laboratory; Reference Range: 24-56 nmol/hr/mg; *Reference Range: 5.1-9.2 nmol/hr/mL; AGA: α-galactosidase A



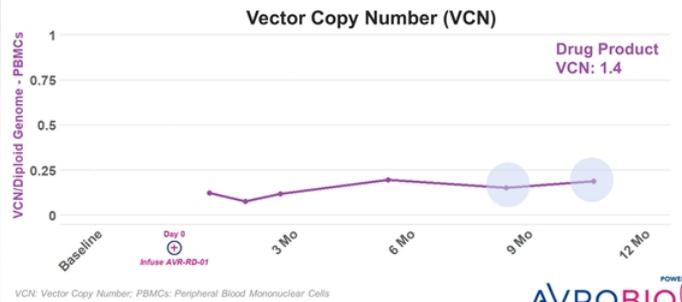
*Reference Value: 2.4 nM; *Reference Value: 4961 nM; Lyso-Gb3: Globotriaosylsphingosine; Gb3: Globotriaosylceramide



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

Skin Biopsy Score (Patient 3)

Baseline	2
6 months	2



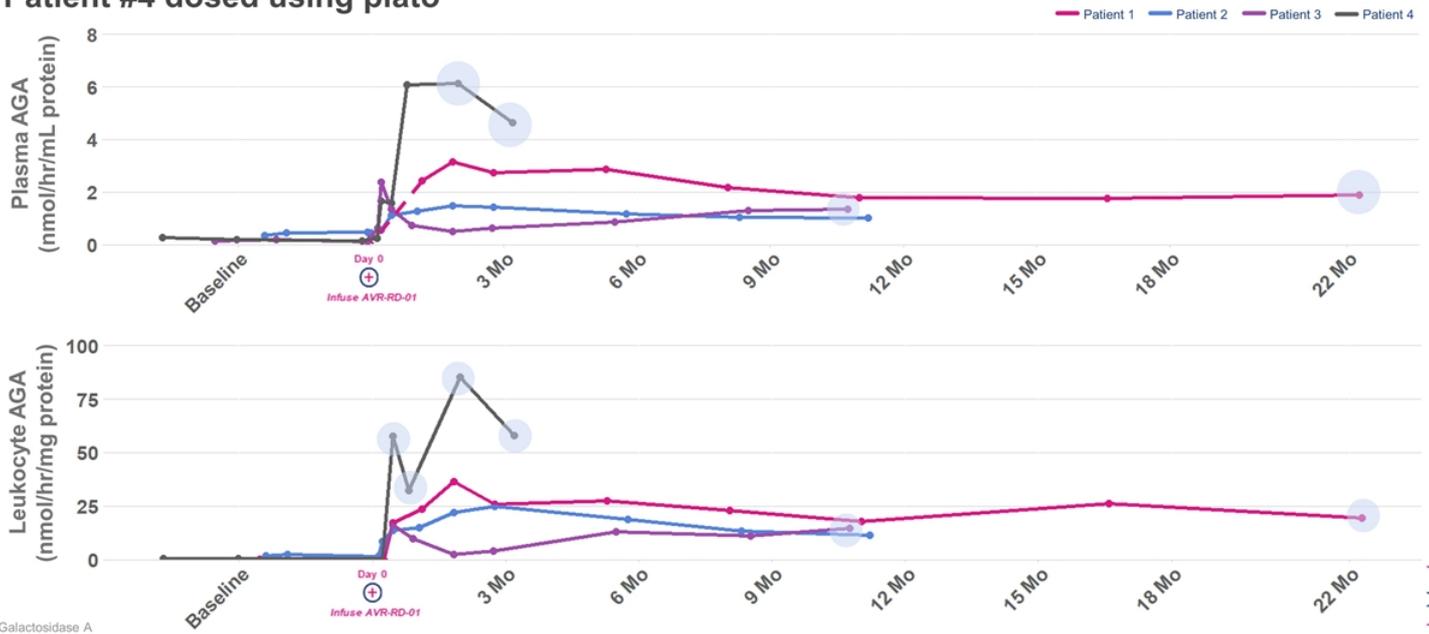
VCN: Vector Copy Number; PBMCs: Peripheral Blood Mononuclear Cells

Note: Visualization of multiple biomarkers adjusted to utilize the same statistical scaling ratio across biomarkers (as compared to prior presentation)
*1-year follow-up = 48 weeks per protocol



Patients 1-4: Plasma and leukocyte enzyme activity sustained up to 22 months

Patient #4 dosed using plato™

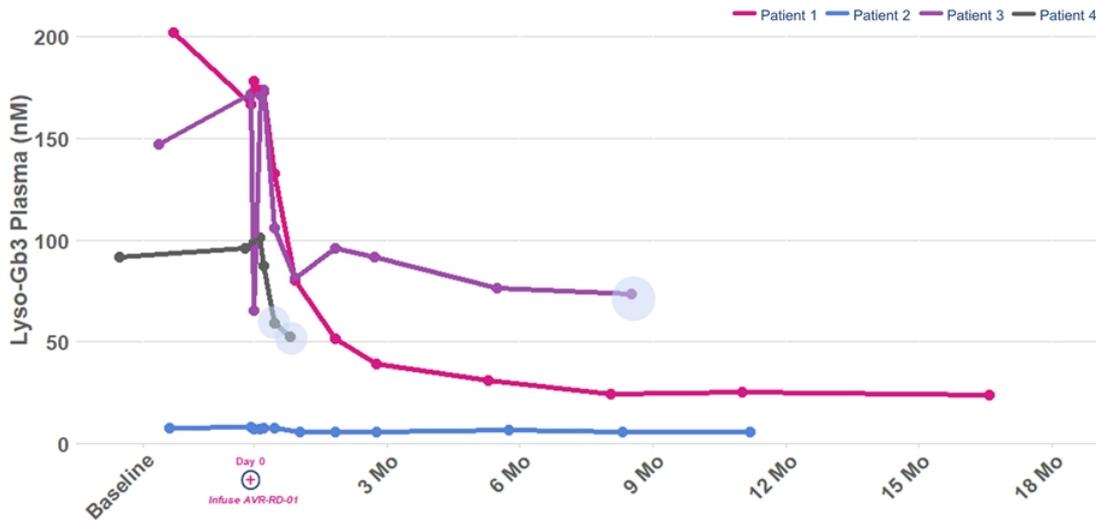


AGA: α -Galactosidase A





Patients 1-4: Plasma lyso-Gb3 reduction sustained up to 18 months



Reduction from Baseline to Last Observation

Patient 1 88%

Patient 2 NA

Patient 3 50%

Patient 4 43%

• Lyso-Gb3: Globotriaosylsphingosine
 • Note: Patient #2 has normal substrate, consistent with late-onset cardiac variant phenotype



Two AVR-RD-01 Fabry clinical trials

9 patients dosed across Phases 1 and 2



PHASE 1

Investigator-Sponsored Trial*

Patients

n = 5 (fully enrolled)
On ERT > 6 months prior to enrollment
18-50 year-old males

Key Objectives

Safety and preliminary efficacy

PHASE 2

AVRO – FAB-201 Trial

Patients

n = 8-12 (4 patients dosed to-date)
Treatment-naive
16 - 50 year-old males



Key Objectives

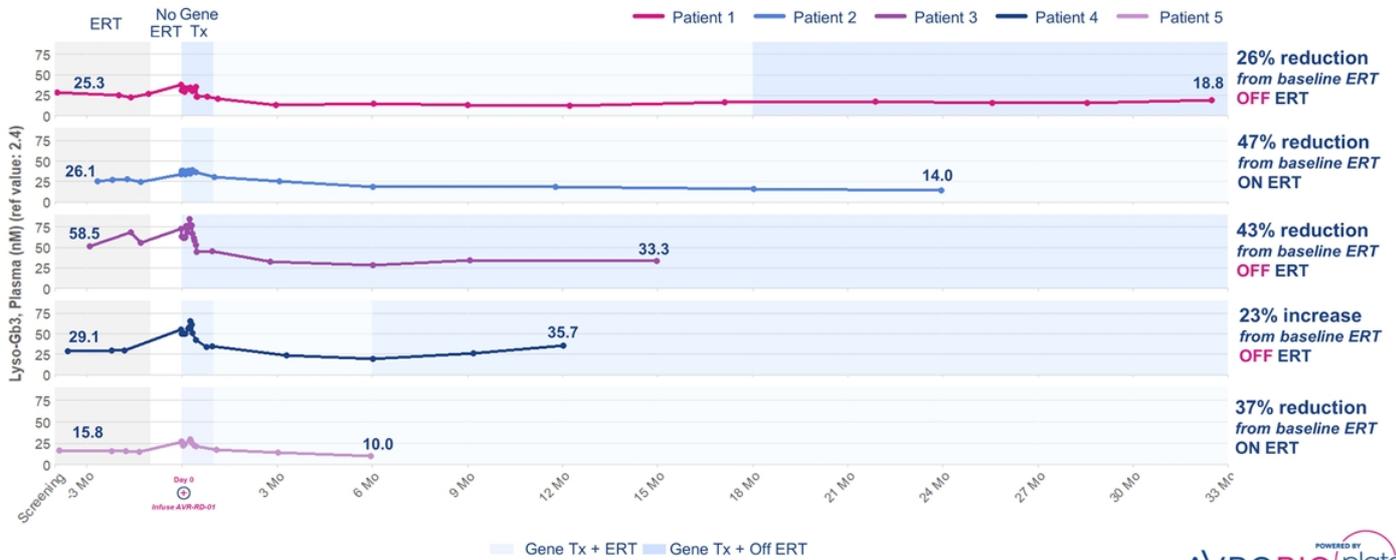
Safety and efficacy

FAB-201 = AVRO-RD-01-201 Study
* Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada
ERT: Enzyme Replacement Therapy



Patients 1-5: Plasma lyso-Gb3 reduction sustained up to 32 months

All patients who have discontinued ERT remain off ERT*



* As of April 27, 2020 (update)
Lyso-Gb3: Globotriaosylsphingosine; ERT: Enzyme Replacement Therapy; Tx: Therapy



Patients 1-5: Leukocyte and plasma enzyme activity sustained up to 32 months

Consistent trends across all patients, 4 patients > 1 year

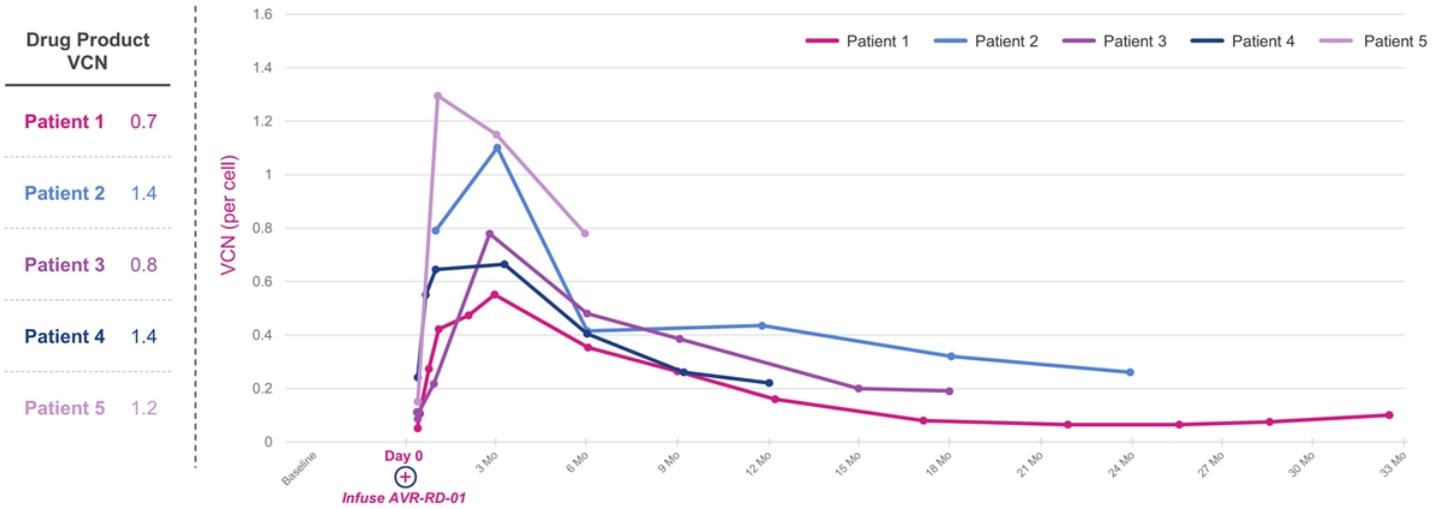


AGA: α -Galactosidase A



VCN stable at 32 months with consistent trend across all other patients

4 patients with 1+ years data



Note: 0.1 VCN is indicative of approx. 5-10% of all nucleated cells having an average of 1-2 copies of the transgene
 VCN: Vector Copy Number



Patient 1: Kidney function stable at 32 months



eGFR: Estimated Glomerular Filtration Rate; ERT: Enzyme Replacement Therapy; TX: Therapy; CKD: Chronic Kidney Disease



Phase 1 Fabry (5 patients) and
FAB-201 (4 patients)

**No unexpected
safety events
or trends
identified**



No SAEs related to AVR-RD-01 drug product



AEs and SAEs reported

Phase 1 AEs (n = 128):

- Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions

FAB 201 AEs (n = 98):

- Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
 - Grade 1 or 2 (n = 72)
 - Grade 3 or 4 (n = 30)

Phase 1SAEs (n = 2):

- Febrile neutropenia (grade 3)
- Thrombophlebitis (grade 2)

FAB 201 SAEs: (n = 4)

Pre-treatment and prior to conditioning

- Seizure (grade 2)

Post-treatment

- Dehydration, nausea, vomiting (grade 3)
- Febrile neutropenia (2 patients, grade 3 & 4)



Anti-AGA antibodies

- Pre-existing low titers detected in 4 patients

Note: Safety data cut November 26, 2019
AE: Adverse Event; SAE: Serious Adverse Event
NOTE: AVR-RD-01 is an investigational gene therapy



Cystinosis



AVR-RD-04



Goals for gene therapy in cystinosis

UNMET NEEDS:



Kidney function

Unmet needs: renal Fanconi syndrome, proteinuria, chronic kidney disease, kidney failure



Vision

Unmet needs: corneal cystine accumulation, photophobia, involuntary eyelid closure



Endocrine disorders

Unmet needs: softening/weakening of bones, bone pain, rickets, long bone deformations, hypophosphatemia, delayed growth, hypothyroidism, pancreatic insulin insufficiency, diabetes, infertility



CNS complications

Unmet needs: myopathy, hypotonia, tremors, difficulty swallowing, neurodevelopmental issues (speech and walking delay and cognitive impairment)



Everyday burden of illness and life expectancy

Unmet needs: medications multiple times per day that cause GI discomfort and sulfur body and breath smell, shortened lifespan

Sources: Ariceta G et al, *Nephrol Dial Transplant*, 2015; Elmonem M et al, *Orphanet Journal of Rare Diseases*, 2016; Gahl et al, *NEJM*, 2002; Bois et al, *J Med Genet*, 1976
CNS: Central Nervous System; GI: Gastrointestinal

Investigator-sponsored* study of AVR-RD-04 in cystinosis patients

First patient dosed



PHASE 1/2

Investigator-Sponsored Trial*

Patients

Up to 6 patients
Adults and adolescents
Cohorts 1-2 ≥ 18 years; Cohort 3 ≥ 14 years
Male and Female
On oral and ophthalmic cysteamine

Key Objectives

Safety and efficacy

* Sponsored by University of California, San Diego
Note: AVR-RD-04 aka CTNS-RD-04



Cystinosis AVR-RD-04 Phase 1/2 Patient Characteristics

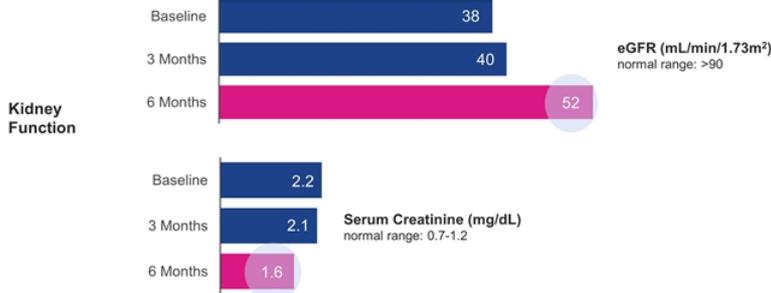
	PATIENT 1
Age of symptom onset / diagnosis	0 year / 8 months
Age dosed with AVR-RD-04	20 years
Gender	Male
Mutation	Allele 1: LDM ₁ Allele 2: Nt1035 (insC)
Primary disease signs and SoC treatment related symptoms, including	<ul style="list-style-type: none">• Fanconi syndrome• Polyuria• Corneal abnormalities• Mild photophobia• Vomiting
Granulocyte Cystine levels at baseline (nmol half cystine per mg protein)*	7.8
Comments	NO kidney transplant <ul style="list-style-type: none">• Cysteamine 1125 mg p.o. every 12 h/day since 2009; discontinued prior to AVR-RD-04 infusion• Cysteamine eyedrops 4-5x/day• Concomitant medications not listed

Note: AVR-RD-01 aka CTNS-RD-04



Patient 1: Initial data indicate positive trends across multiple measures

CLINICAL LAB MEASURES



BIOMARKER ENDPOINTS



- Experimental *in vivo* confocal microscopy
- Two skin areas, behind the ear and 'optional', averaged
- Analysis and quantification (3D Image-Pro software)

VCN (vcni/dg) (Drug Product = 2.1)

1 Month	2.9
2 Months	3.0
3 Months	2.0

Average Granulocyte Cystine Level (µmol half cystine/g protein)

Baseline	7.8
1 Month	1.3
2 Months	1.5
3 Months	1.5

Asymptomatic Heterozygous Carrier Granulocyte Cystine Range: 0.2 – 1.9 µmol half cystine/g protein

Source: Gertsman I et al., Clinical Chemistry, 2016

VCN: Vector Copy Number; CTNS: Cystinosis, Lysosomal Cystine Transporter; mRNA: Messenger Ribonucleic Acid; eGFR: Estimated Glomerular Filtration Rate; SCR: Serum Creatinine

*Data obtained using a novel experimental methodology utilizing *in vivo* confocal microscopy, to image crystals in the skin behind the ear



Patient 1: Reduced treatment burden at 6 months

Number of Medications and Supplements

(max per day)

Before Gene Therapy

ON Cysteamine



52

After Gene Therapy

(at 6 months post-gene therapy)

OFF Cysteamine



NOTE: Investigational gene therapy



Phase 1/2 Cystinosis
1 patient dosed

**No unexpected
safety events
or trends
identified**



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



No SAEs reported



AEs reported

- Consistent with myeloablative conditioning and underlying disease
- N = 22 (moderate = 9, mild = 13)

Pre-treatment and prior to conditioning (n = 6, not all events listed)

- Diarrhea, hypokalemia, dizziness
- Dehydration, vomiting

Post-treatment (n = 16, not all events listed)

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

Note: Safety database cut as of January 27, 2020
AE: Adverse Event; SAE: Serious Adverse Event



plato™

—
AVROBIO's foundation designed to
scale gene therapy worldwide

*State-of-the-art technologies including
automated manufacturing platform*

+ Optimized
for performance

+ Redefines manufacturing
best practices

AVROBIO POWERED BY plato



plato™: Three upgrades designed to optimize potency, safety and durability



UPGRADES	Increase enzyme activity	Increase transduction efficiency	Increase VCN	Increase marrow space / engraftment	Increase consistency and safety
1 Vector	+	+	+		
2 Conditioning			+	+	+ *
3 Automation	+				+

Upgrades designed to increase Vector Copy Number (VCN), enzyme activity, chimerism and durability

* TDM (therapeutic drug monitoring)

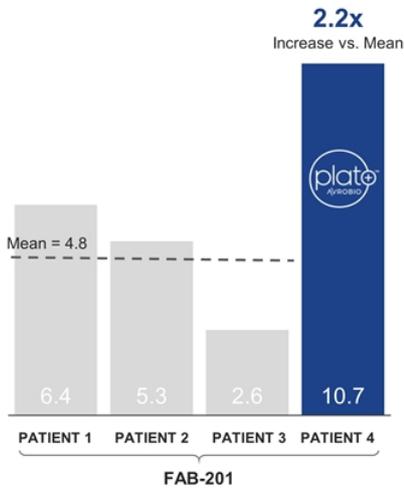
VECTOR UPGRADE:

Metrics compared to academic process

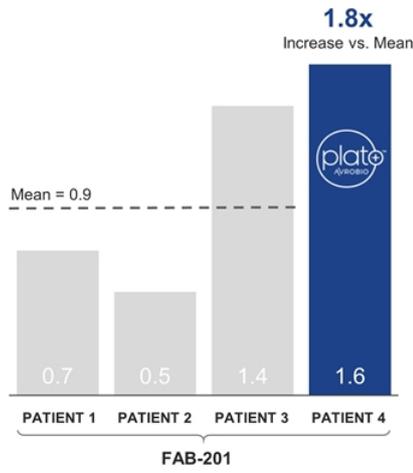
FAB-201 patient #4 drug product data with plato™



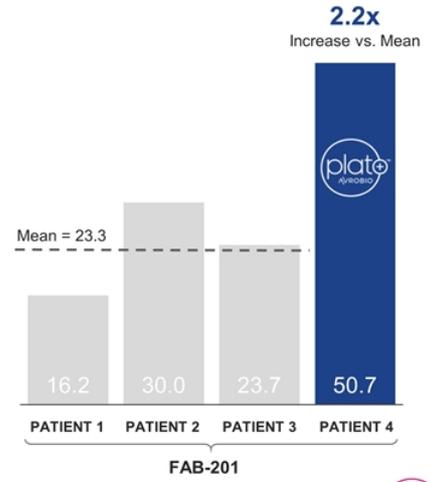
Enzyme Activity (nmol/hr/mL)



VCN (per diploid genome)



Transduction Efficiency (%)



VCN: Vector Copy Number; FAB-201: AVR-RD-01 Study
NOTE: Data is from drug product



VECTOR UPGRADE:

Metrics compared to academic process

FAB-201 and AVR-RD-04 drug product data



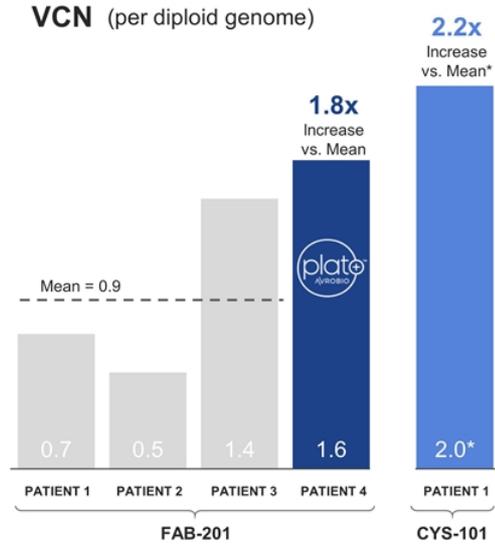
FAB-201 with plato™

- 4-plasmid vector (LV2)
- Bu TDM conditioning
- Automated manufacturing

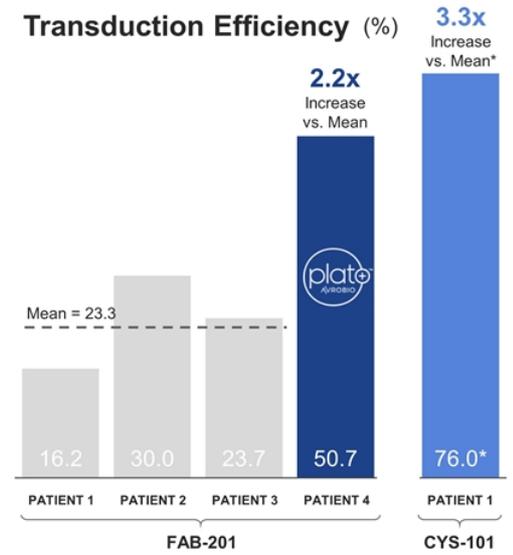
AVR-RD-04 with “plato-like”

- 4-plasmid vector
- Bu TDM conditioning
- Manual manufacturing

VCN (per diploid genome)



Transduction Efficiency (%)



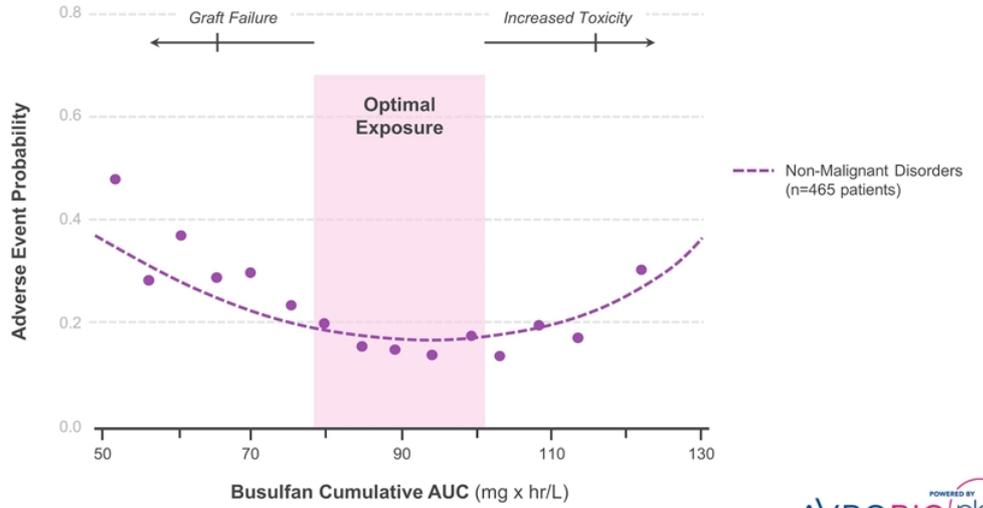
BU TDM: Busulfan Therapeutic Drug Monitoring; VCN: Vector Copy Number; FAB-201: AVR-RD-01 Study; CYS-101: AVR-RD-04 Study; LV: Lentiviral Vector
 * Manufactured at UCLA using UCLA's assays and methodologies
 NOTE: Data is from drug product



PRECISION CONDITIONING UPGRADE:
Targeted busulfan intended to balance optimal engraftment with enhanced safety
Meta-analysis of 465 patients identified optimal exposure

Optimized precision dosing designed to enhance tolerability

Lowest rate of adverse events in the Bu90 range



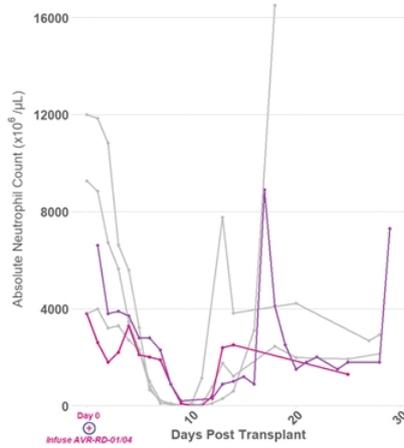
Bu: Busulfan; AUC: Area Under the Curve
 Sources: Bartelink LH et al, Lancet Haematol, 2016

PRECISION CONDITIONING UPGRADE: Rapid neutrophil and platelet recovery with minimal lymphocyte depletion using Busulfan TDM

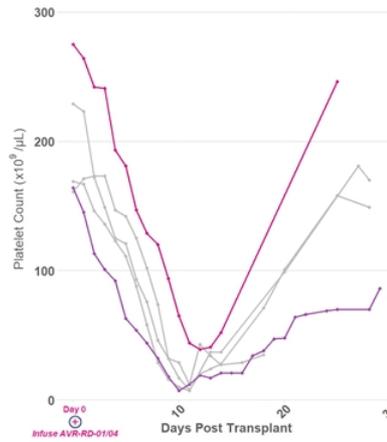
New
data
point



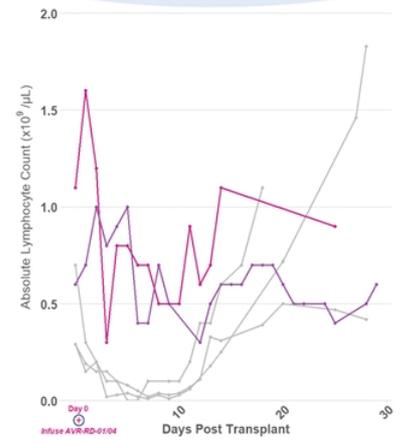
Absolute Neutrophil Count (ANC)



Platelet Count



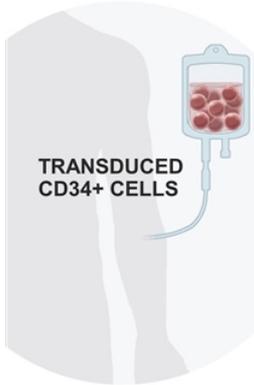
Absolute Lymphocyte Count



— Cystinosis Patient 1: Busulfan — Fabry Patients 1 – 3: Mel — Fabry Patient 4: Bu90-TDM

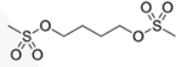
Fabry: Patients #1-3 Melphalan 100mg/m2; Patient #4 Busulfan 'AUC 90'; Cystinosis: Patient #1 Busulfan 'AUC 90'
 Threshold levels for prophylactic supportive care in HSC Tx; ANC $<0.5 \times 10^9$ per liter (AABB); Platelets $<10 \times 10^9$ cells/L (AABB)
 NOTE: Neutrophil counts - G-CSF administration post gene therapy: Pt 1: 7 Doses, Day 7 – 14, Pt 2: 11 Doses, Day 7 – 17, Pt 3: 6 Doses, Day 7 – 12, Pt 4: 5 Doses, Day 8 – 12
 NOTE: Platelet counts - Platelet Transfusion: Pt 1: Day 10; Pt 2, 3: Day 11, Pt 4: no transfusion
 TDM = Therapeutic Drug Monitoring; G-CSF = Granulocyte-colony stimulating factor

PRECISION CONDITIONING UPGRADE:
Designed to access “hard-to-reach”
compartments



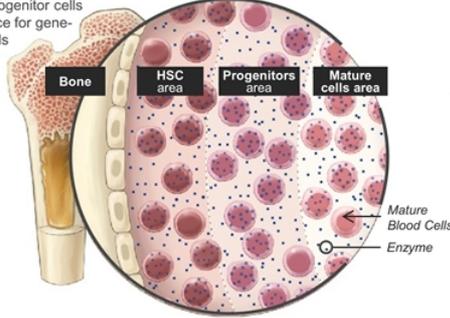
BRAIN

Busulfan crosses blood-brain barrier and eliminates resident microglia cells making space for gene-modified cells

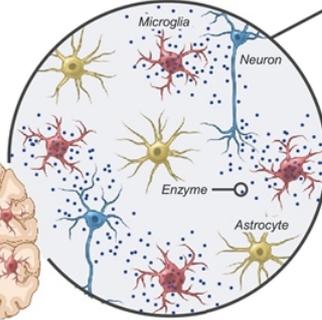


IN THE BONE MARROW

Busulfan eliminates hematopoietic (CD34+) stem and progenitor cells making space for gene-modified cells

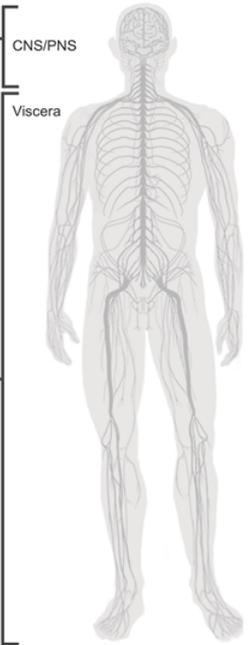
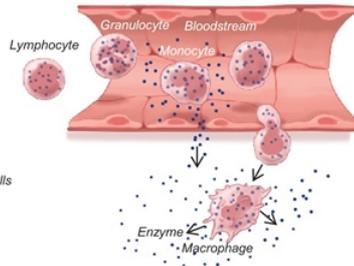


MICROGLIA
Potential for widespread microglia engraftment throughout the brain



BONE MARROW

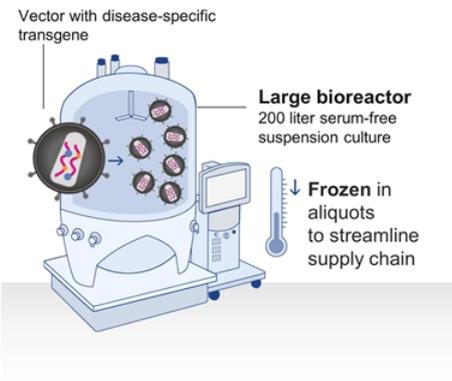
PERIPHERAL TISSUE



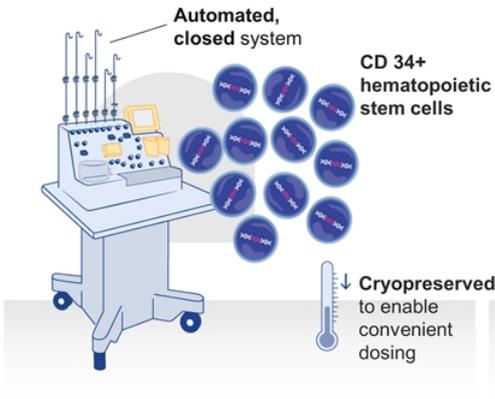
AUTOMATION UPGRADE:
Designed to deliver large-scale manufacturing
Differentiated, cost-effective approach



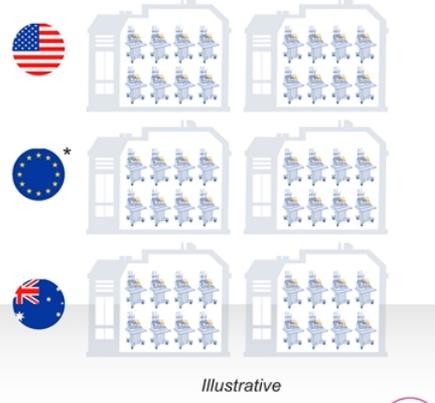
HIGH VOLUME / TITRE



INCREASE CONSISTENCY



COST-EFFECTIVE SCALE-OUT

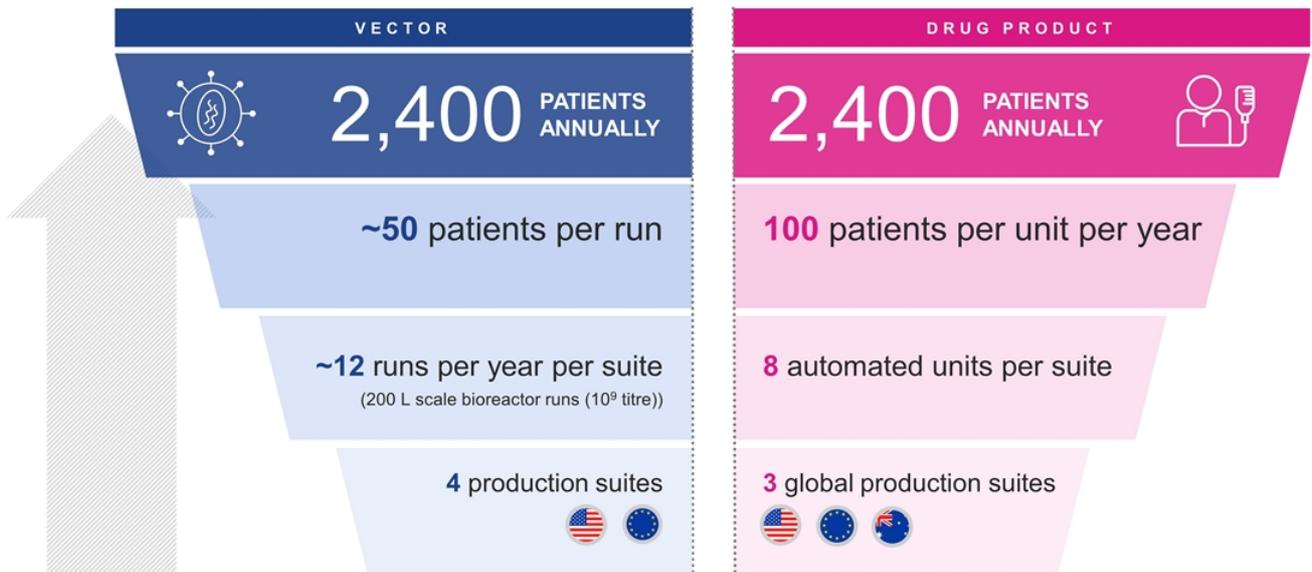


* European manufacturing capabilities planned for 2H 2020; manufacturing capabilities currently in place in U.S. & Australia

AUTOMATION UPGRADE:

Poised to manufacture at scale

Designed to optimize potency and safety, and overcome historic CMC bottlenecks



Illustrative



3 UPGRADES IN PLACE:

New data point

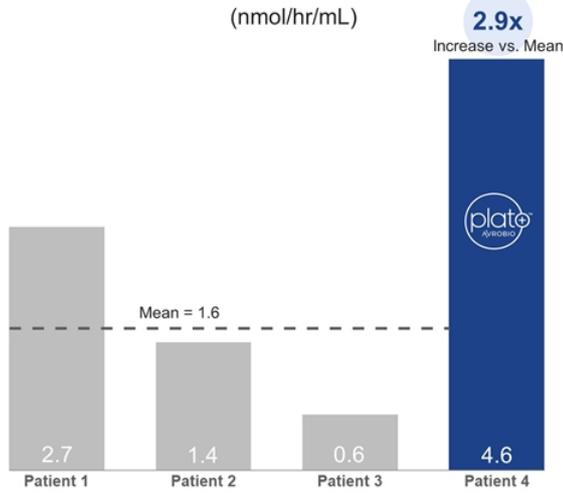


plato™ metric compared to academic process

FAB-201 THREE MONTH data for patient #4 with plato™ vs. patients #1-3

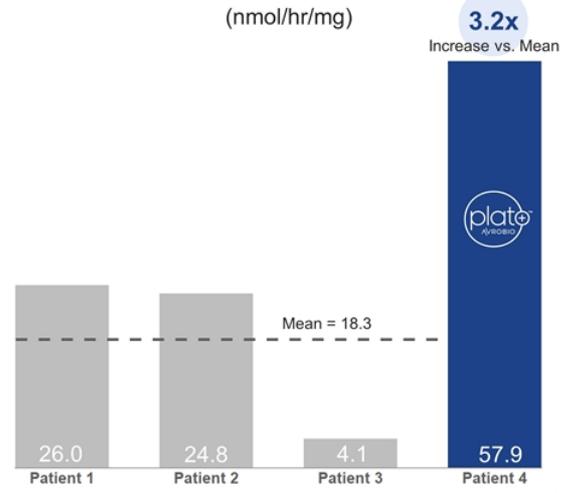
Plasma Enzyme Activity

(nmol/hr/mL)



Leukocyte Enzyme Activity

(nmol/hr/mg)



ASGCT 2020 data update – key takeaways



New data show consistent results across Fabry disease and cystinosis programs

Long-term Fabry patient data

Sustained long-term positive trends

- Patient 1 in the Phase 2 trial continues to show stable leukocyte and plasma AGA enzyme activity, now out 22 months
- Patient 3 in the Phase 2 trial shows increased leukocyte and plasma AGA enzyme activity, decreased plasma lyso-Gb3 level, and stable VCN at new time points
- All three Phase 1 patients off ERT remain off ERT

First Fabry plato™ patient

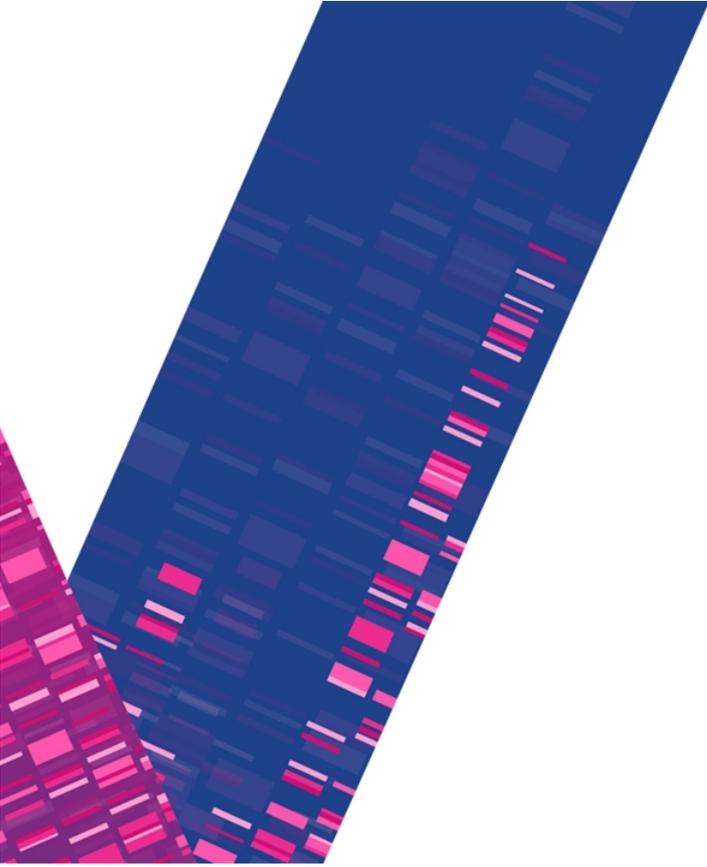
plato continues to perform

- One-month plasma lyso-Gb3 decrease of 43% vs. baseline
- Three-month leukocyte and plasma enzyme activity levels 3x greater than mean of other three patients at same timepoint in Phase 2 trial
- Rapid neutrophil and platelet recovery with minimal lymphocyte depletion post Bu90 conditioning

Cystinosis Patient 1 data

Positive trends at six months, including kidney function measures

- eGFR and serum creatinine measures trending positively at 6 months
- Pill burden remains significantly lower than at baseline

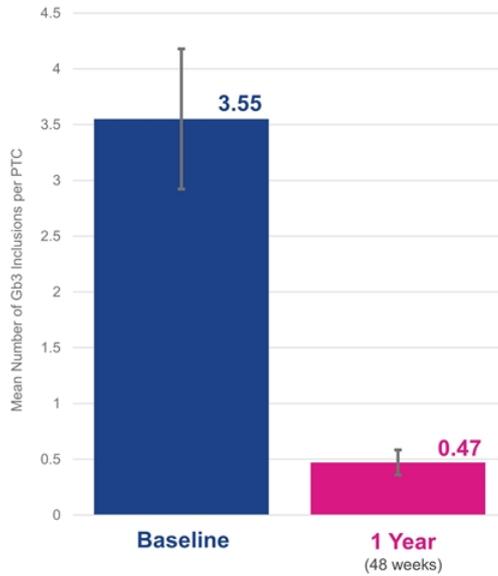


Appendix



Patient 1: 87% substrate reduction in kidney biopsy at 1 year

Average number of **Gb3** inclusions per peritubular capillary (PTC)



- Unpaired t-test for difference between $n=55$ PTCs at baseline vs. $n=101$ PTCs at 1 year; $p < 0.0001$
- Error bar represents the standard deviation

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
 FAB-201-1: First patient in FAB-201 clinical trial
 PTC: Peritubular Capillary; Gb3: Globotriaosylceramide; GL-3: Globotriaosylceramide; KIC: Kidney Interstitial Capillary

New collaborations advancing leadership in lentiviral gene therapy



Fully Automated Bu-TDM Immunoassay

- AVROBIO and Saladax announced agreement to develop and validate Saladax's fully automated nanoparticle immunoassay kit
- Designed to work on most automated hospital analyzers
- Regular technician, 24/7 analysis possible with results anticipated in minutes using only microLs of blood
- Designed to analyze 10-100s samples per machine/hour
- Expected to eliminate Bu degradation errors as assay conducted in real-time at the point of care
- Scalable



Antibody-Drug Conjugate

- AVROBIO and Magenta announced research & clinical collaboration agreement to evaluate Magenta's preclinical CD117-targeted antibody conjugate to amanitin (MGTA-117) in conjunction with AVROBIO investigational gene therapies
- Designed to deplete only hematopoietic stem and progenitor cells
- Has shown promising data in non-human primates
- MGTA-117 currently in IND-enabling studies
- Each party retains commercial rights to its own programs

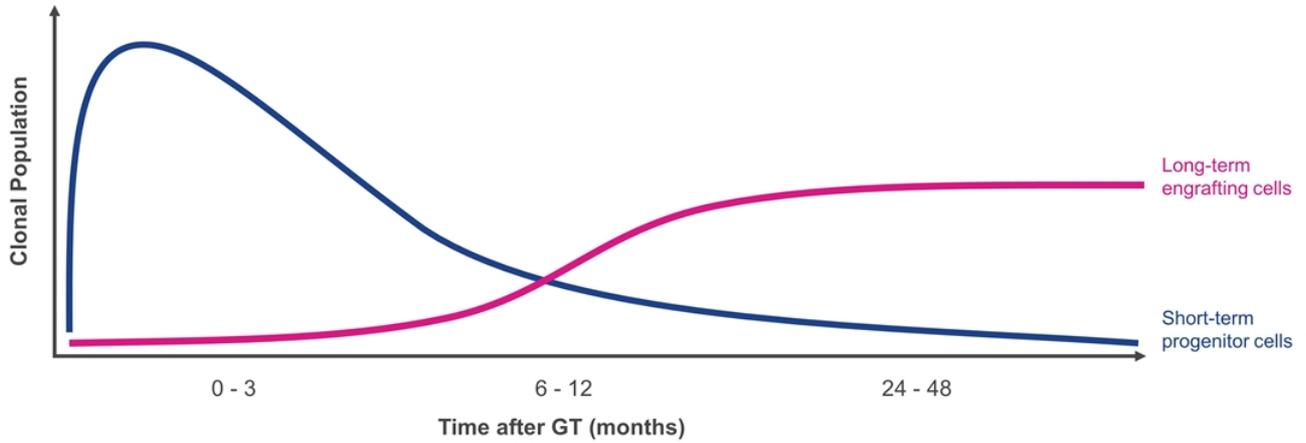




Hematopoietic reconstitution occurs in two distinct phases

A few thousand long-term engrafting cells stably sustain levels of transgene product

First wave of short-term progenitor cells start to exhaust with progressive takeover by a smaller population of long-term engrafting cells



Source: Blasco L et al, Cell Stem Cell, 2016

AVROBIO Reports Updated Clinical Data from Investigational Gene Therapy Programs for Fabry Disease and Cystinosis

Sustained enzyme activity up to 22 months and consistent trends demonstrated across multiple other measures in first patient in Fabry disease Phase 2 clinical trial

Data from first patient treated using plato™ gene therapy platform in Fabry disease trial show:

- *43-percent reduction in toxic metabolite plasma lyso-Gb3 one month post-treatment*
- *Significantly higher leukocyte and plasma enzyme activity three months post-treatment than other Phase 2 patients treated using academic platform at same timepoint*

Data from first cystinosis patient in Phase 1/2 trial show positive trends at six months, including in kidney function measures

CAMBRIDGE, Mass., May 13, 2020 — **AVROBIO, Inc.** (Nasdaq: AVRO), a leading clinical-stage gene therapy company with a mission to free people from a lifetime of genetic disease, today announced new clinical data from its investigational programs for Fabry disease and cystinosis. The data will be presented today at the American Society of Gene & Cell Therapy (ASGCT) 23rd Annual Meeting.

“We’re excited to see continued strong results across our clinical programs for Fabry disease and cystinosis. The general consistency across our Phase 2 Fabry disease patients treated so far suggests that a one-time dose of our investigational gene therapy may enable patients to durably produce the functional enzyme they need to clear toxic substrates and metabolites. Additionally, six months post-treatment, the first patient in our investigator-sponsored Phase 1/2 trial for cystinosis continues to show positive trends for important measures of kidney function,” said Geoff MacKay, AVROBIO’s president and CEO. “We’re gratified to see plato™ continuing to perform, with the first patient treated using plato’s personalized conditioning regimen of busulfan with therapeutic drug monitoring (TDM) reporting a significant reduction in plasma lyso-Gb3 one month post-treatment. At three months, this patient’s leukocyte and plasma enzyme activity were triple the levels seen at the same timepoint in the other Phase 2 patients, who were treated using our academic platform rather than plato.”

New interim data continue to support potential first-line use of AVR-RD-01 for Fabry disease

Four patients have been dosed in the Phase 2 trial (FAB-201) of AVR-RD-01, AVROBIO’s investigational lentiviral gene therapy for Fabry disease. The following new data will be presented today at ASGCT:

- The first patient continued to show increased leukocyte and plasma AGA enzyme activity, now up to 22 months post-treatment. These data suggest the patient is producing an

endogenous supply of functional alpha-galactosidase (AGA) enzyme, which is essential to prevent the accumulation of a toxic metabolite, lyso-Gb3, in tissues including the heart and kidneys. A sustained decrease in plasma lyso-Gb3 and total Gb3 levels has previously been reported for this patient out to 18 months.

- The third patient had a sustained decrease in plasma lyso-Gb3 and total Gb3 levels nine months after dosing. This patient also had a stable vector copy number (VCN) out approximately one year post-treatment, suggesting successful engraftment.
- The fourth patient, who is also the first to be dosed with AVROBIO's plato gene therapy platform, had a 43-percent reduction in the toxic metabolite plasma lyso-Gb3 at one month. At three months, he also had leukocyte enzyme and plasma enzyme activity levels approximately three times higher than the mean activity level of the first three patients in the same trial at the same timepoint.

While the presentation today will focus on data updates for its Phase 2 trial, the company also reports that all three Phase 1 patients who discontinued enzyme replacement therapy (ERT) after receiving AVR-RD-01 gene therapy, remain off ERT as of April 27, 2020.

As of the safety data cut-off date of Nov. 26, 2019, there have been no safety events attributed to AVR-RD-01 drug product in either the Phase 1 or Phase 2 trial. Through the safety data cut-off date, four serious adverse events (SAEs) have been reported in the FAB-201 trial and two SAEs in the Phase 1 trial. The fourth Phase 2 patient, who was dosed after the safety data cut-off date, has reported an SAE, which was not attributed to AVR-RD-01 and which subsequently resolved. Across both studies, each of the SAEs has been consistent with the conditioning regimen, stem cell mobilization, underlying disease or pre-existing conditions. Pre-existing low anti-AGA antibody titers have been detected in four patients in the Phase 1 trial and a transient low titer was observed but not detectable in subsequent measures in one patient in the Phase 2 trial.

AVROBIO continues to actively identify participants for the Phase 2 Fabry disease trial in Australia, Canada and the U.S. The FAB-201 trial is an ongoing open-label, single-arm Phase 2 clinical trial evaluating the efficacy and safety of AVR-RD-01 in eight to 12 treatment-naïve Fabry disease patients.

New six-month data for cystinosis program indicate positive trends in key kidney function measures

New data will also be presented from the first patient dosed in the investigator-sponsored Phase 1/2 trial of AVR-RD-04 for cystinosis, a progressive disease marked by the accumulation

of cystine in cellular organelles known as lysosomes. This buildup can cause debilitating symptoms including kidney failure, corneal damage and thyroid dysfunction, often leading to a shortened lifespan. Currently, more than 90 percent of treated cystinosis patients require a kidney transplant in the second or third decade of life. The current standard of care for cystinosis is cysteamine, a burdensome treatment regimen that can require dozens of pills per day and may not prevent overall progression of the disease.

Six months following administration of AVR-RD-04, the patient's estimated glomerular filtration rate (eGFR), which is a measure of kidney function, improved from 38 mL/mi/1.73m² at baseline to 52 mL/mi/1.73m². The patient's serum creatinine, another measure of kidney function, also improved, falling from 2.2 mg/dL at baseline to 1.6 mg/dL at six months. The patient stopped cysteamine treatment before administration of AVR-RD-04 and remains off cysteamine.

As of the safety data cut-off date of Jan. 27, 2020, which was approximately three months following administration of the investigational gene therapy to the first patient in the AVR-RD-04 program, there have been no reports of safety events attributed to the investigational drug product. In addition, no SAEs have been reported as of the safety data cut-off date. Adverse events did not suggest any unexpected safety signals or trends.

The cystinosis data will be presented today at ASGCT by Stephanie Cherqui, Ph.D., an associate professor at the University of California, San Diego (UCSD), the principal investigator of the trial and an AVROBIO collaborator and consultant. The Phase 1/2 trial of AVR-RD-04 is funded by grants to UCSD from the California Institute for Regenerative Medicine, Cystinosis Research Foundation and the National Institutes of Health (NIH). The trial is actively identifying up to six participants.

About AVROBIO's personalized gene therapy approach

Our investigational lentiviral gene therapies start with the patient's own stem cells. We use a lentiviral vector to transduce those cells in order to insert a therapeutic gene designed to enable the patient to produce a functional supply of the protein they lack. These cells are then infused back into the patient, where they are expected to engraft in the bone marrow and produce generations of daughter cells, each containing a copy or copies of the therapeutic gene. To optimize engraftment, we use a personalized conditioning regimen of busulfan with therapeutic drug monitoring (TDM) to clear space in the patient's bone marrow. Our approach is designed to drive durable production of the functional protein throughout the patient's body, thereby potentially addressing symptoms from "head to toe," including those originating in the central nervous system.

About lentiviral gene therapy

Lentiviral vectors are differentiated from other delivery mechanisms because of their large cargo capacity and their ability to integrate the therapeutic gene directly into the patient's chromosomes. This integration is designed to maintain the therapeutic gene's presence as the patient's cells divide, which potentially enables dosing of pediatric patients, whose cells divide rapidly as they grow. Because the therapeutic gene is integrated using the vector into patients' stem cells ex vivo, patients are not excluded from receiving the investigational therapy due to pre-existing antibodies to the viral vector.

About AVROBIO

Our mission is to free people from a lifetime of genetic disease with a single dose of gene therapy. We aim to halt or reverse disease throughout the body by driving durable expression of functional protein, even in hard-to-reach tissues and organs including the brain, muscle and bone. Our clinical-stage programs include Fabry disease, Gaucher disease and cystinosis and we also are advancing a program in Pompe disease. **AVROBIO** is powered by the plato™ gene therapy platform, our foundation designed to scale 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 Statement

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 prospective product candidates, the design, commencement, enrollment and timing of ongoing or planned clinical trials, clinical trial results, product approvals and regulatory pathways, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, timing and likelihood of success, the expected benefits and results of our implementation of the plato platform in our clinical trials and gene therapy programs, and the expected safety profile of our investigational gene therapies. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Results in preclinical or early-stage clinical trials may not be indicative of results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

Any forward-looking statements in this press release are based on AVROBIO's current expectations, estimates and projections about our industry as well as management's current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of AVROBIO's product candidates 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 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 materially and adversely from those contained in the forward-looking statements, see the section entitled "Risk Factors" in AVROBIO's most recent Quarterly Report, as well as discussions of potential risks, uncertainties and other important factors in AVROBIO's subsequent filings with the Securities and Exchange Commission. AVROBIO explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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