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): July 15, 2019

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 July 15, 2019, AVROBIO, Inc. (the "Company") issued a press release titled "AVROBIO Announces 87% Substrate Reduction in First Kidney Biopsy and Additional Positive Data from Clinical Trials of AVR-RD-01 Investigational Gene Therapy in 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.

On July 15, 2019, 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 Press release issued by AVROBIO, Inc., dated July 15, 2019.

99.2 AVROBIO, Inc. slide presentation, dated July 15, 2019.

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: July 15, 2019

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

AVROBIO Announces 87% Substrate Reduction in First Kidney Biopsy and Additional Positive Data from Clinical Trials of AVR-RD-01 Investigational Gene Therapy in Fabry Disease

- 87% reduction in average number of Gb3 inclusions in first kidney biopsy taken one year post-treatment, the primary efficacy endpoint in the Phase 2 trial
- Plasma lyso-Gb3 consistently reduced 33% to 41% below baseline enzyme replacement therapy (ERT) levels in the first four Phase 1 patients
- Durability observed across multiple biomarkers, sustained at more than two years for the first Phase 1 patient
- No SAEs related to AVR-RD-01 drug product; SAEs and AEs reported have been consistent with conditioning regimen, underlying disease or pre-existing conditions across both studies
- Company to host a conference call to discuss these additional data today, July 15, 2019, at 8:00 a.m. ET

CAMBRIDGE, Mass.– July 15, 2019 – AVROBIO, Inc. (NASDAQ: AVRO) (the "Company") today announced the first kidney biopsy result and additional positive data from two ongoing clinical trials of its AVR-RD-01 investigational gene therapy in Fabry disease. To date, eight patients have been dosed in the trials – three patients in the Phase 2 FAB-201[1] trial and five patients in the Phase 1 FACTs[2] trial.

AVR-RD-01 Summary of Interim Clinical Data

The primary efficacy endpoint for the Phase 2 FAB-201 trial is the change from baseline in the average number of Gb3 inclusions per peritubular capillary (PTC)[3] as measured in a kidney biopsy one year post-treatment with AVR-RD-01. Gb3, or globotriaosylceramide, is a substrate (or fat) that accumulates in the cells of Fabry patients and can result in damage to multiple organs including the kidneys and heart.

In addition to safety, the FAB-201 and Phase 1 clinical trials are examining a number of secondary efficacy and other endpoints, including biomarkers, such as measurements in the plasma of Gb3 and lyso-Gb3 (the toxic metabolite of Gb3), AGA enzyme activity levels in leukocytes and plasma, vector copy number (VCN), as well as indicators of kidney and cardiac function.

The following is a summary of key observations from the most recent interim clinical data set:

- *Substantial Gb3 substrate reduction in kidney biopsy.* The kidney biopsy for the first treatment-naïve patient dosed in the FAB-201 trial, as reviewed by two independent examiners, showed a reduction from an average of 3.55 Gb3 inclusions per PTC at baseline to an average of 0.47 inclusions per PTC one year after administration of the Company's AVR-RD-01 investigational gene therapy, representing an 87% reduction.
- *Sustained plasma lyso-Gb3 reductions.* The first Phase 2 patient had an 87% reduction in plasma lyso-Gb3 at one year. The first four Phase 1 patients have seen their plasma lyso-Gb3 levels reduced between 33% and 41% versus their ERT pre-treatment levels. In particular, the 41% reduction level has stabilized at more than two years for the first Phase 1 patient.

- *Durability data for AVR-RD-01 continues to show sustained results across multiple parameters.* All six patients across the trials for whom data are reported at six months or longer post-treatment with AVR-RD-01 show sustained AGA enzyme activity in leukocytes and plasma and exhibit consistent VCN trends, with VCN levels for the first Phase 1 patient stable at more than two years post-treatment.
- *Kidney and cardiac functions stable.* Kidney and cardiac functions, as measured by GFR[4] and cardiac MRI Left Ventricular Mass parameters, were stable and in a normal range in the first Phase 2 patient at one year.
- *Phase 1 patients who have discontinued ERT remain off ERT.* The two patients in the Phase 1 trial who discontinued ERT post-AVR-RD-01 treatment remain off ERT to date. These patients have now been off ERT for 10 and 9 months, respectively. A third patient is in the process of discontinuing ERT.
- *No unexpected trends or safety events were identified.* Serious adverse events (SAEs) and adverse events (AEs) reported were generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions.

“We are excited by the magnitude of the Gb3 reduction observed in the first patient’s kidney biopsy at 12 months. This is the primary efficacy endpoint in FAB-201 and an efficacy endpoint that has previously been utilized by the FDA in evaluating and approving treatment for Fabry disease,” commented Birgitte Volck, MD, PhD, AVROBIO’s President of Research and Development. “Our prior data readouts have shown AVR-RD-01 is associated with reductions of Gb3 and lyso-Gb3 levels in the plasma, and today’s data further support its potential to reduce Gb3 levels in tissue, including in the kidney. We believe the 87% Gb3 clearance in the kidney biopsy may be considered clinically relevant since Gb3 accumulation in organs of Fabry patients is associated with significant morbidity and early mortality.”

Dr. Mark Thomas of the Department of Nephrology at Royal Perth Hospital and Clinical Professor at the University of Western Australia Medical School, the lead investigator for the FAB-201 trial, noted, “I believe today’s data indicate that AVR-RD-01 is substantially reducing the build-up of Gb3 substrate in kidney tissue to potentially effective clearance levels. This, along with the sustained reduction in Gb3 and lyso-Gb3 in plasma observed to date, could translate into substantially improved patient outcomes over the current standard of care.”

Interim clinical data for all eight patients dosed to date in the FAB-201 and Phase 1 clinical trials appear to indicate that the Company’s AVR-RD-01 investigational gene therapy has been generally well tolerated with no unexpected trends or safety events identified. No serious adverse events (SAEs) related to the AVR-RD-01 drug product were reported as of the safety data cut-off dates of July 10, 2019 for the FAB-201 trial and May 24, 2019 for the Phase 1 trial. As of the respective safety data cut-off dates, four SAEs were reported in the FAB-201 trial and two SAEs were reported in the Phase 1 trial and were consistent with expectations for the myeloablative conditioning regimen, stem cell mobilization, underlying Fabry disease, or pre-existing conditions. Low anti-AGA antibody titers have been detected in two patients, one in each of the trials, and the Company believes neither is considered to be of clinical relevance.

“With eight Fabry patients across two trials now treated with our investigational gene therapy, we are extremely pleased with the emerging data set and its support for AVR-RD-01 to potentially address the genetic basis of Fabry disease. As these clinical trials progress, we aim to position AVR-RD-01 as a first-line therapy,” said Geoff MacKay, AVROBIO’s President and CEO. “Looking beyond Fabry disease, we remain on track for other important anticipated milestones, including the dosing of the first patients in the Gaucher and cystinosis Phase 1/2 trials in the second half of 2019 as well as the introduction into our clinical programs of our commercial-scale plato platform.”

Enrollment in the FAB-201 clinical trial is ongoing, and further details are available on clinicaltrials.gov.

Conference Call and Webcast Information

AVROBIO will host a conference call and webcast on Monday July 15, 2019 at 8:00 a.m. ET to review the updated clinical data. The event will be webcast live and can be accessed under “Events and Presentations” in the Investors section of the Company’s website at www.avrobio.com. Alternatively, audience members may listen to the call by dialing (866) 353-0165 from locations in the United States and (409) 217-8080 from outside the United States. The conference ID number is 1578335. A replay of the webcast will be available on the Company’s website for 90 days following the call.

About Fabry Disease

Fabry disease is a rare lysosomal storage disease associated with significant morbidity and early mortality. It is caused by a defective gene that causes a deficiency in the functional enzyme, α-galactosidase A (AGA), which breaks down a particular type of fat in the body’s cells known as globotriaosylceramide, or Gb3. As Gb3 and related substrates build up in patients with Fabry disease, Gb3 and its metabolites (principally lyso-Gb3) become toxic to the patient’s cells. The accumulation of Gb3 and other glycosphingolipids results in damage to multiple tissues and organs, especially the kidneys, heart and blood vessels, leading to cerebrovascular complications including stroke. In addition, high levels of Gb3 substrate accumulation in the kidney may cause kidney failure. Gb3 can also accumulate in other tissues, such as the nervous system, where it can lead to debilitating pain. Due to end-stage renal disease and other life-threatening complications associated with Fabry disease, the average life expectancy in affected classic Fabry males is approximately 58 years of age. Most patients with Fabry disease begin experiencing chronic pain in childhood but are often not diagnosed with Fabry disease until their twenties, due to a broad variation in patient symptoms. It is estimated that Fabry disease is diagnosed in approximately one in 40,000 males and one in 118,000 females in the United States, but studies have suggested that a larger number of patients may be undiagnosed.

About the AVR-RD-01 Clinical Trials

The investigator-sponsored Phase 1 trial is designed to assess the safety and preliminary efficacy of the Company's investigational gene therapy, AVR-RD-01, in patients with classic Fabry disease who have been treated with standard-of-care enzyme replacement therapy (ERT) for at least six months; enrollment is complete with five patients dosed. The Phase 1 trial is conducted by the FACTs team (FAbry disease Clinical research and Therapeutics) in Canada and led by their principal investigator, Jeffrey A. Medin, PhD. 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 twelve treatment-naïve patients with Fabry disease.

About AVR-RD-01

AVR-RD-01 is an investigational, ex vivo lentiviral gene therapy being developed as a single-dose therapy with the potential to provide life-long therapeutic benefit for patients with Fabry disease. AVR-RD-01 employs a state-of-the-art lentiviral vector system that is designed to be an efficient gene transfer system with the goal of permanent integration of functional copies of the AGA transgene[5] into the patient's own stem cells. In patients with Fabry disease, hematopoietic stem cells are collected from the patient and then transduced with lentiviral vector carrying a functional version of the α-galactosidase A (GLA) gene that encodes for active α-galactosidase A (AGA) – the enzyme that is deficient in Fabry disease – to create AVR-RD-01. AVR-RD-01 is then infused back into the patient with the goal of having transduced cells, and their daughter cells, secrete functional AGA into the plasma and tissues, which can then be taken up by other cells in the body. This process is called cross correction.

About AVROBIO, Inc.

AVROBIO, Inc. is a leading, Phase 2 gene therapy company focused on the development of its investigational gene therapy, AVR-RD-01, in Fabry disease, as well as additional gene therapy programs in other lysosomal storage disorders including Gaucher disease, cystinosis and Pompe disease. The Company's plato™ platform includes a proprietary vector system, automated cell manufacturing solution and refined conditioning regimen deploying therapeutic drug monitoring. AVROBIO is headquartered in Cambridge, MA and has offices in Toronto, ON. For additional information, visit www.avrobio.com.

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 such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words 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 product candidates, the design, 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, the expected safety profile of our product candidates and timing and likelihood of success of current or future product candidates. 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 realize the intended benefits of our gene therapy 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, 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, 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.

1 The official name of the 'FAB-201 Trial' is AVRO-RD-01-201, which is a Phase 2 trial of AVROBIO's investigational gene therapy, AVR-RD-01, in Fabry disease.

2 FACTs - FAbry disease Clinical research and Therapeutics in Canada is conducting the Phase 1 trial. Jeffrey A. Medin, PhD, Vice Chair of Research Innovation and MACC Fund Chair of Pediatrics and Biochemistry, Medical College of Wisconsin, is the Principal Investigator of the FACTs team.

3 Peritubular capillaries (PTCs), also referred to as kidney interstitial capillaries (KICs), convey blood after filtration in the glomeruli, enabling it to eventually exit the kidneys and return to the circulatory system.

4 Glomerular Filtration Rate (GFR) includes estimated GFR (eGFR) determined using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, and measured GFR (mGFR) determined using plasma clearance of iohexol.

5 A transgene is an exogenous DNA sequence introduced into the genome, which in the case of AVR-RD-01 encodes for functional AGA enzyme.

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Exhibit 99.2

AVROBIO

Freedom from a lifetime of disease

July 15, 2019

Disclaimer

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

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Any forward-looking statements in this presentation are based on 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, the risk that AVROBIO may not realize the intended benefits our gene therapy platform, 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 approval 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, 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 Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2019, 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.

AVROBIO

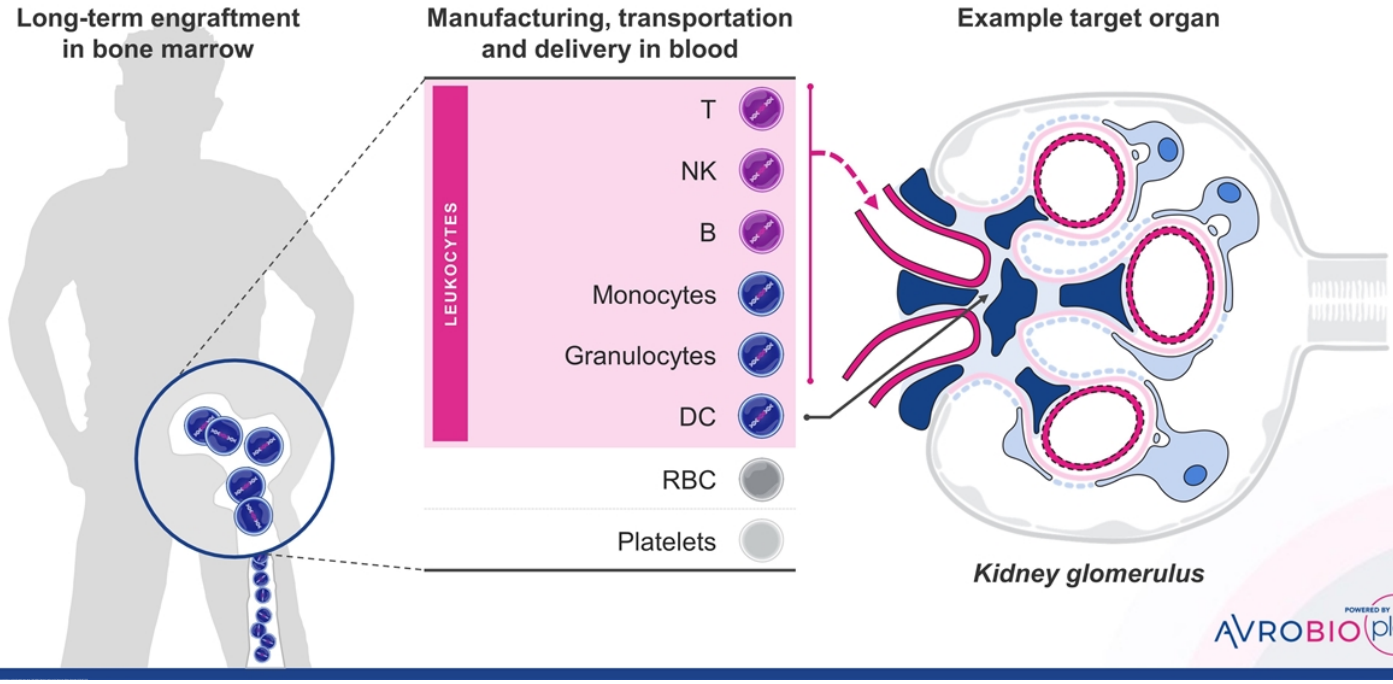
Freedom from a lifetime of disease

July 15, 2019

Key questions for today

- What is the kidney biopsy (primary efficacy endpoint) result for the first patient in FAB-201?
- How well are the 5 Fabry patients in Phase 1 doing versus baseline ERT?
- What have we learned about the durability of AVR-RD-01?
- Will the Gaucher and cystinosis trials start in 2019?
- What is the status of our ongoing transition to plato™?

Endogenous enzyme delivered to tissues via multiple cell lineages



Two AVR-RD-01 Fabry clinical trials

8 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 (3 patients dosed to-date)
Treatment-naive
16 - 50 year-old males

Key Objectives

Safety and efficacy

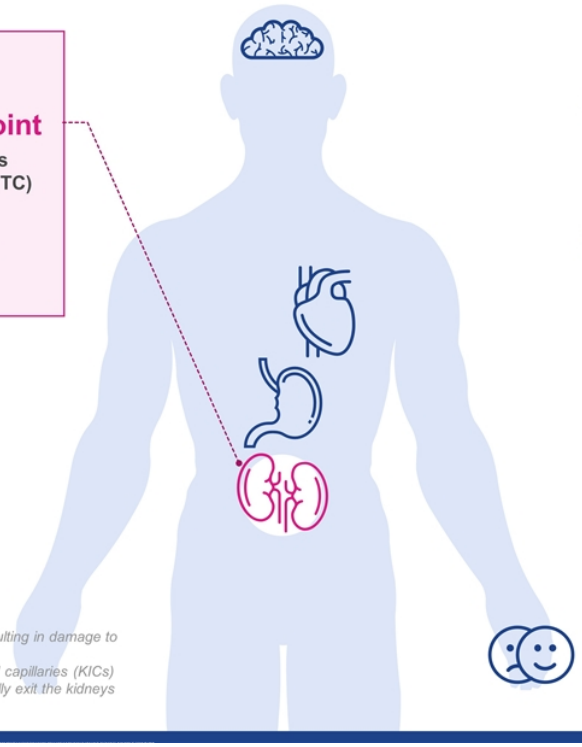
** Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada*

FAB-201 Primary and secondary endpoints

FAB-201
Primary efficacy endpoint

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

- Biopsy at 1 year vs. baseline
- FDA-recognized endpoint in Fabry



Primary safety endpoints

AEs, SAEs
Clinical labs, ECG, vital signs
Antibodies, RCL, ISA

Secondary efficacy endpoints

ORGAN AND SYSTEM FUNCTION
Kidney function
Cardiac function
GI distress
Pain

PATIENT WELL-BEING
Clinical status
Quality of life

BIOMARKERS
Toxic metabolite – lyso-Gb3 in plasma, urine
Substrate – Gb3 in plasma, urine, skin
Enzyme – AGA in leukocytes, plasma
VCN

Gb3, also referred to as GL-3: a type of fat that builds in cells, resulting in damage to kidneys, heart and brain
Peritubular capillaries (PTCs), also referred to as kidney interstitial capillaries (KICs) convey blood after filtration in the glomeruli, enabling it to eventually exit the kidneys and return to the circulatory system

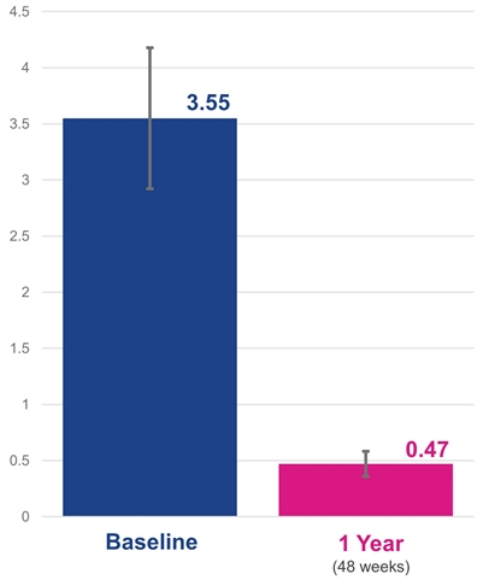
FAB-201 Patient Characteristics

	PATIENT 1	PATIENT 2	PATIENT 3
Age symptom onset / diagnosis	10 / 19 years	36 / 37 years	13 / 13 years
Age dosed with AVR-RD-01	21 years	46 years	40 years
Mutation	c.1021G>A (p.E341K)	c.644A>G (p.N215S)	c.639+1G>T
Primary disease signs and symptoms	• Kidney disease • Chronic pain • GI symptoms • Decreased cold sensation	• Cardiac disease • Peripheral neuropathy • Chronic pain • Increased tiredness • GI symptoms • Intermittent tinnitus • Mild high frequency hearing loss • Raynaud's syndrome	• Kidney disease • GI symptoms • Peripheral neuropathy • Bilateral deafness • Tinnitus • Peripheral edema • Decreased cold sensation
Leukocyte AGA enzyme activity at baseline (nmol/h/mg)	0.10*	2.38**	0.58**
Plasma lyso-Gb3 at baseline (nM)***	202	8	147
Comment	IgA deposits in kidney biopsy	Cardiac variant, not a classic Fabry male	

* *Mayo Lab, ref range ≥23.1 nmol/h/mg*
** *Rupar Lab, ref range 24-56 nmol/h/mg*
*** *Reference value ≤ 2.4 nM*
Note: *AGA is α-galactosidase A, Lyso-Gb3 is lyso-globotriaosylceramide*

FAB-201 Patient 1: 87% substrate reduction in kidney biopsy

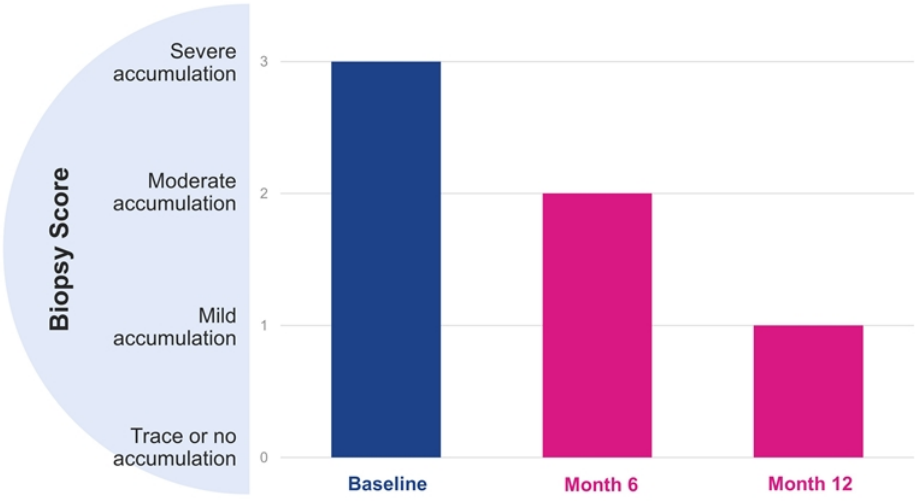
Average number of **Gb3 inclusions per peritubular capillary (PTC)**



- *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*

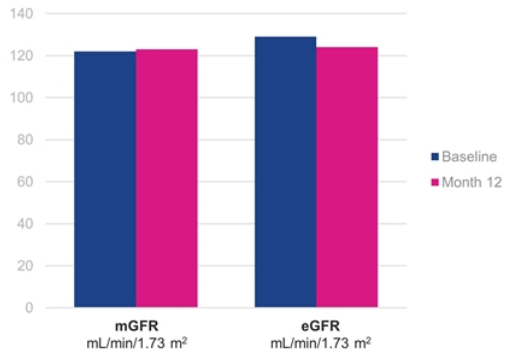
FAB-201 Patient 1: Continued reduction in substrate inclusions in skin endothelial cells



Source: Thurberg BL, 2011, https://everylifefoundation.org/wp-content/uploads/images/workshopseries/16-Thurberg-Fabry-pathology-Nov-2011-compr-dc.pdf

FAB-201 Patient 1: Kidney and cardiac function stable at one year

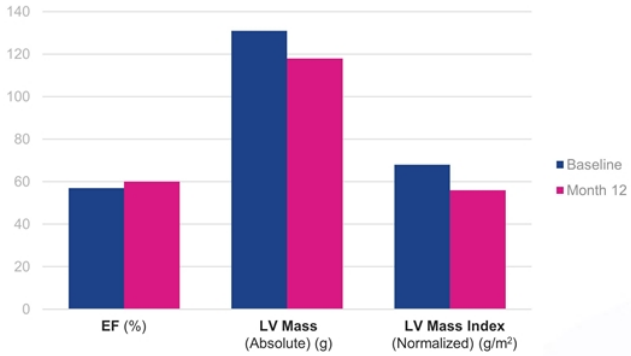
KIDNEY FUNCTION
remains within normal range



Normal Range	mGFR/eGFR
Male (20-29 years)	Average 116*

***Source**: https://www.kidney.org/atoz/content/gfr*
***Note:** mGFR is measured Glomerular Filtration Rate, eGFR is estimated Glomerular Filtration Rate*

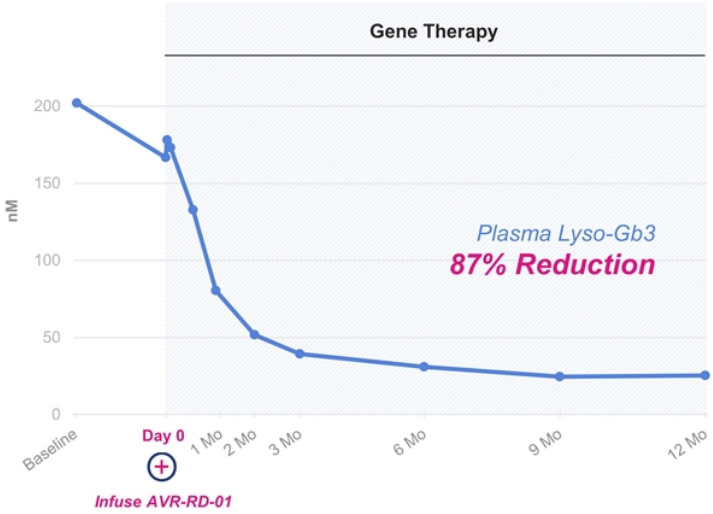
CARDIAC FUNCTION
remains within normal range

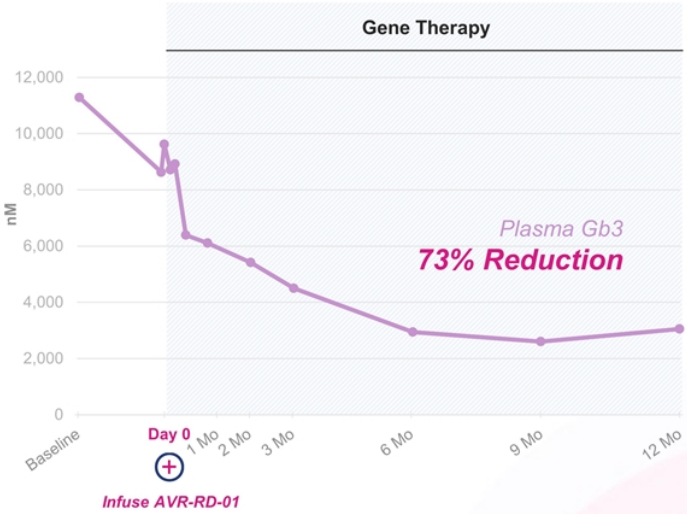


Reference Range Mean Values ± SD	EF (%)	LVM (g)	LVMI (g/m²)
Male (20-39 years)	64.3 ± 4.2	138.9 ± 24.5	67.8 ± 10.7

***Source:** Alfakih K et al, J Magn Reson Imaging, 2003*
***Note:** EF is Ejection Fraction, LVMI is Left Ventricular Mass Index*

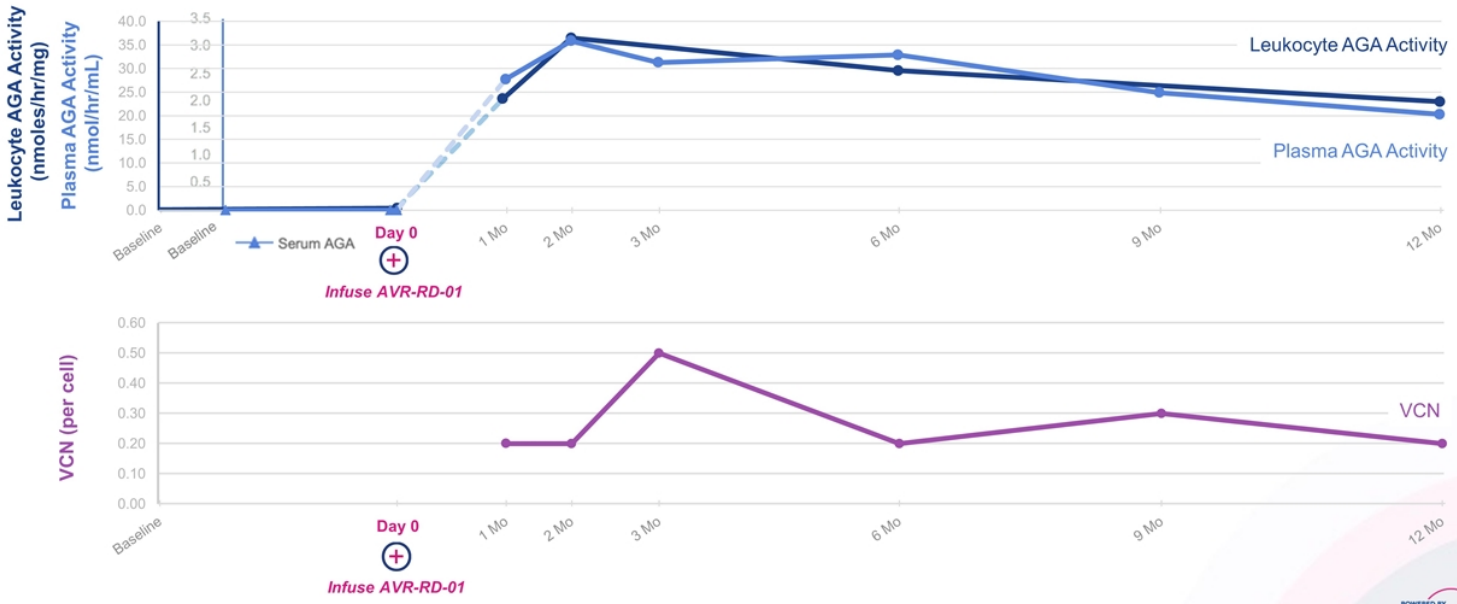
FAB-201 Patient 1: Substantial reduction in plasma substrate / metabolite levels, sustained at 1 year





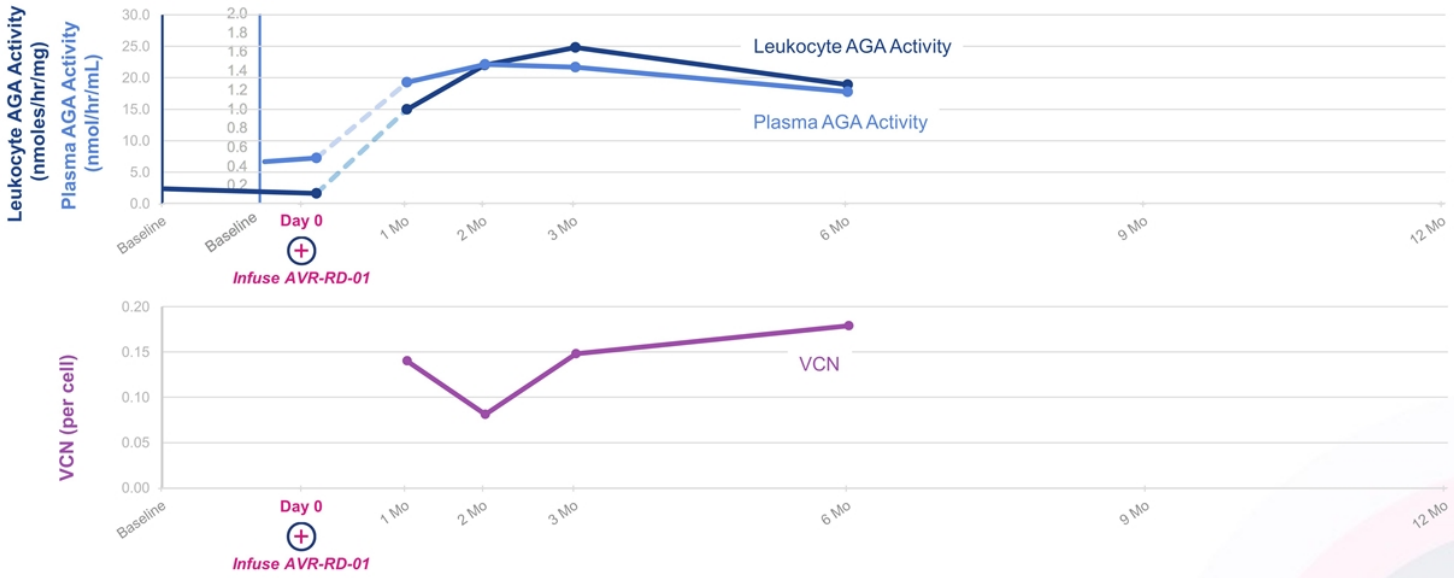
Baseline: *The last available, non-missing observation prior to AVR-RD-01 infusion*
Note: *AVR-RD-01 is an investigational gene therapy*

FAB-201 Patient 1: Sustained leukocyte and plasma enzyme activity at 1 year; VCN stable



Note: 0.1 VCN is indicative of approx. 5-10% of all nucleated cells having an average of 1-2 copies of the transgene
Baseline: *The last available, non-missing observation prior to AVR-RD-01 infusion*

FAB-201 Patient 2: Sustained leukocyte and plasma enzyme activity and VCN at 6 months



Note: *Patient 3 had plasma AGA activity of 0.740, leukocyte AGA activity of 9.94 and VCN of 0.12 as of 1 month*
Note: 0.1 *VCN is indicative of approx. 5-10% of all nucleated cells having an average of 1-2 copies of the transgene*
Baseline: *The last available, non-missing observation prior to AVR-RD-01 infusion*

FAB-201
3 patients dosed

No unexpected trends or safety events identified

No AEs or SAEs related to AVR-RD-01 drug product

AEs and SAEs reported

- **AEs**
  - Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
- **SAEs**
  - **Pre-treatment**
    - Seizure (resolved)
  - **Post-treatment**
    - Dehydration, nausea, vomiting (resolved)
    - Febrile neutropenia (resolved)

Anti-AGA antibodies

- Transient low titer in 1 subject (resolved)

Note: *Safety database cut as of July 10, 2019*

Two AVR-RD-01 Fabry clinical trials

8 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

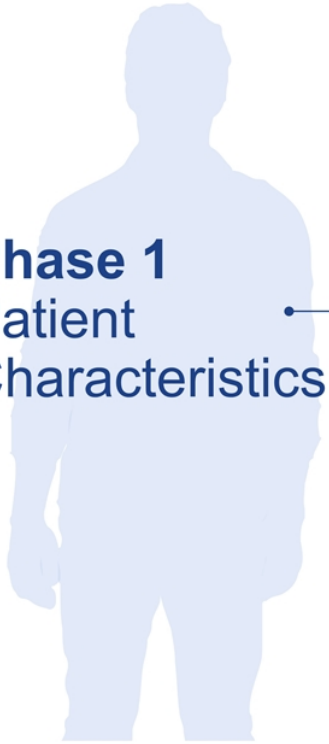
Patients

n = 8-12 (3 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*



Phase 1 Patient Characteristics

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4	PATIENT 5
Age symptom onset / diagnosis	18 / 37	9 / 29	10 / 0	7 / 4	10 / 14
Years on ERT	11	6	4	11	2
Age dosed with AVR-RD-01	48	39	40	37	30
Mutation	c.962A>G (p.Q321R)	c.1033T>C (p.S345P)	c.427G>C (p.A143P)	c.427G>C (p.A143P)	(p.Y134S)
Primary disease signs and symptoms	• Kidney disease • Cardiac disease • GI pain • GI diarrhea • Angiokeratoma • Insomnia	• Kidney disease • Cardiomyopathy • Hypohidrosis • Corneal verticillata • Peripheral neuropathy • GI symptoms • Angiokeratoma • Lymphedema • Acroparesthesia	• Cardiac Disease • Tinnitus • Headaches • Dizziness • Acroparesthesia	• Cardiac Disease • Hypohidrosis • Tinnitus • Corneal verticillata • Angiokeratoma • GI symptoms	• Kidney disease • Hypertension • Hypohidrosis • Tinnitus • Migraines • Impaired hearing • Angiokeratoma • Sleep apnea • Asthma • Depression
Leukocyte AGA activity at baseline* (nmol/h/mg)	2.1	1.1	0.6	2.2	1.0
Plasma lyso-Gb3 at baseline (nM)**	25	26	59	29	16
Discontinued ERT	18 months after gene therapy dose		Did not resume ERT after gene therapy dose	ERT discontinuation planned	

** Rupar Lab, ref range 24-56 nmol/h/mg*
*** Reference value ≤ 2.4 nM*
Note: *AGA is α-galactosidase A, Lyso-Gb3 is lyso-globotriaosylceramide*

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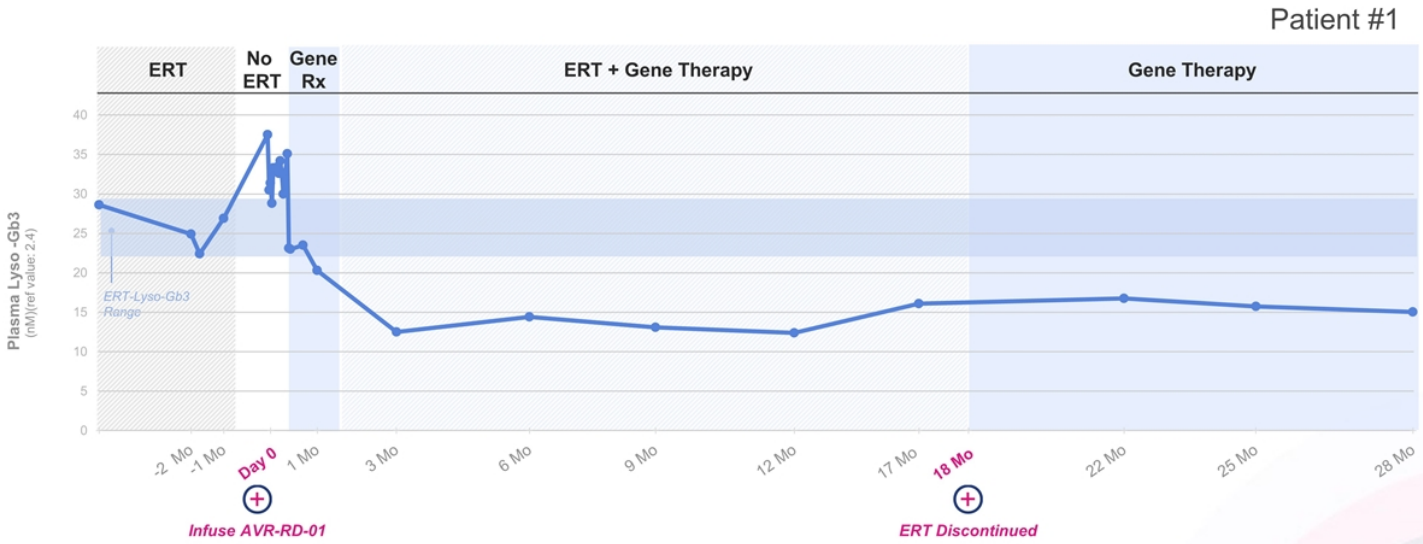
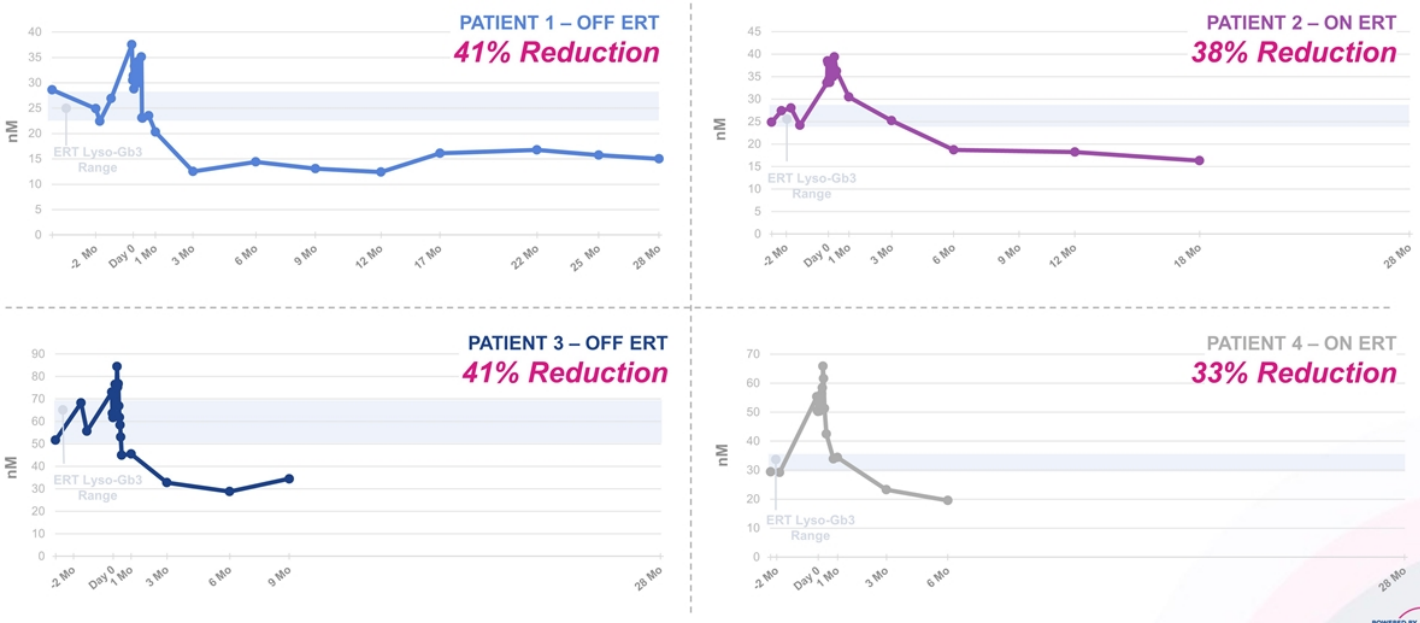
Phase 1: Plasma lyso-Gb3 reduction sustained >2 yrs

Reduced 41% from ERT baseline*



Baseline: The mean of the values reported prior to initiating mobilization
Note: AVR-RD-01 is an investigational gene therapy candidate

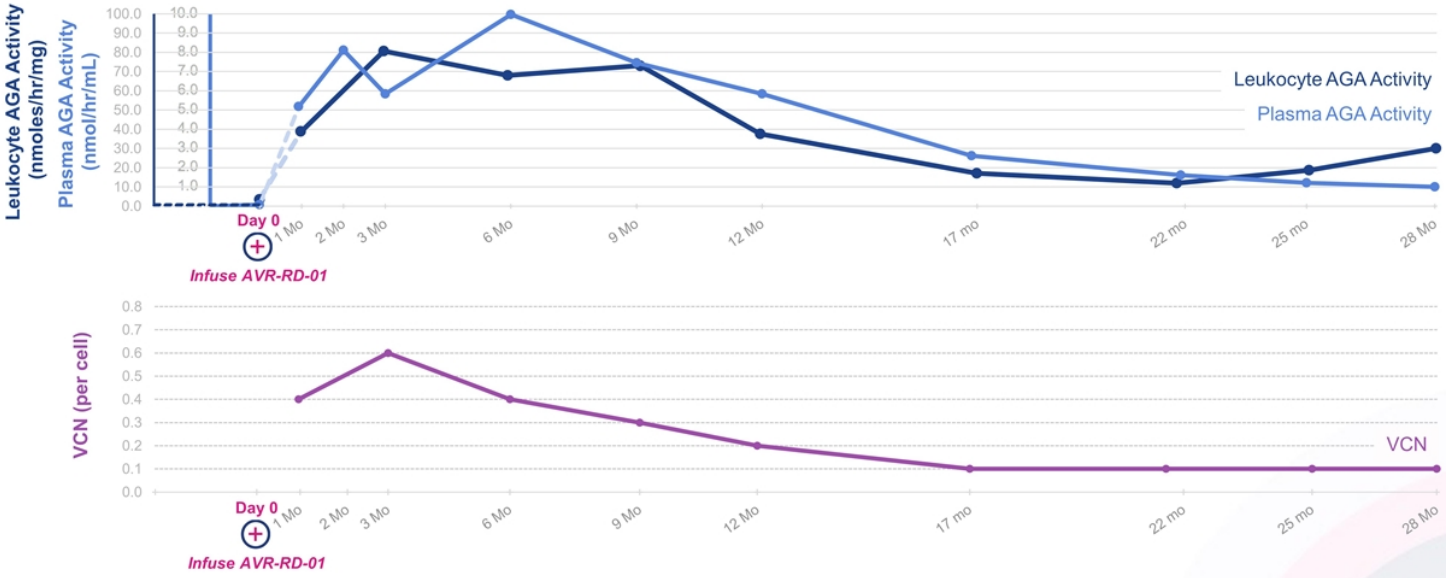
Phase 1: Plasma lyso-Gb3 consistently reduced by 33-41% vs. baseline* ERT



__Baseline:__ The mean of the values reported prior to initiating mobilization
__Percent reduction:__ As measured from baseline to last assessment

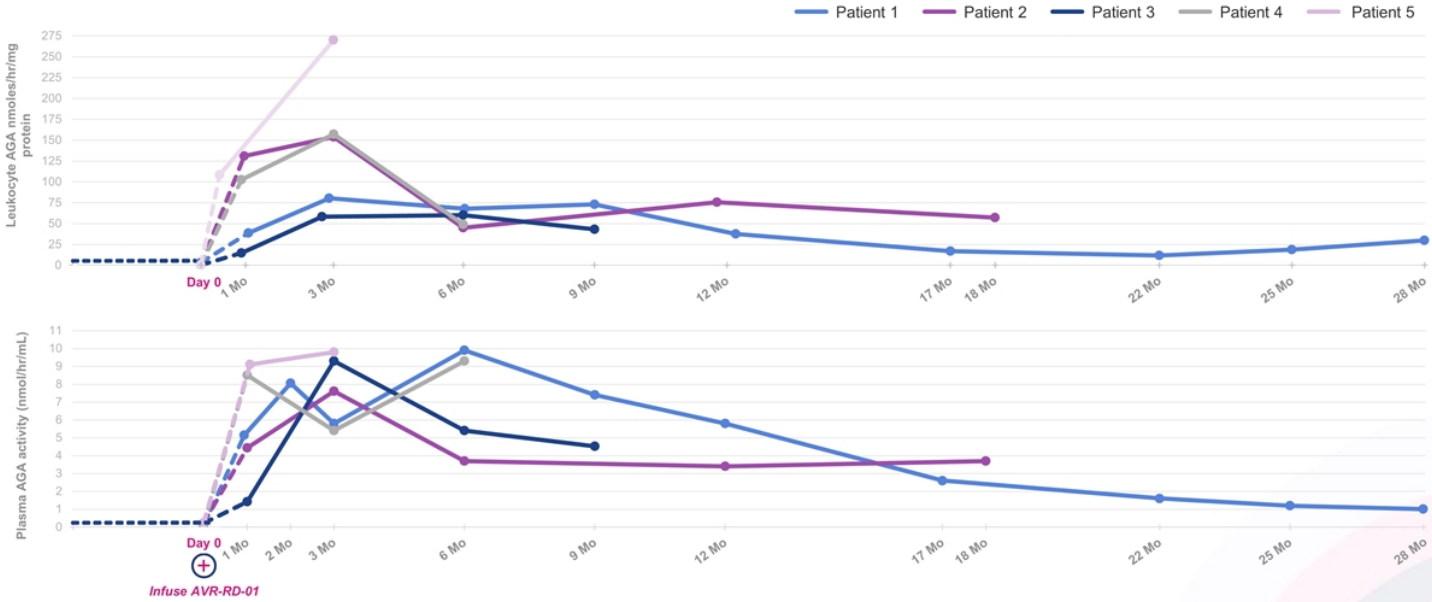
Phase 1: Leukocyte and plasma enzyme activity sustained >2 years; VCN stable

Patient #1



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

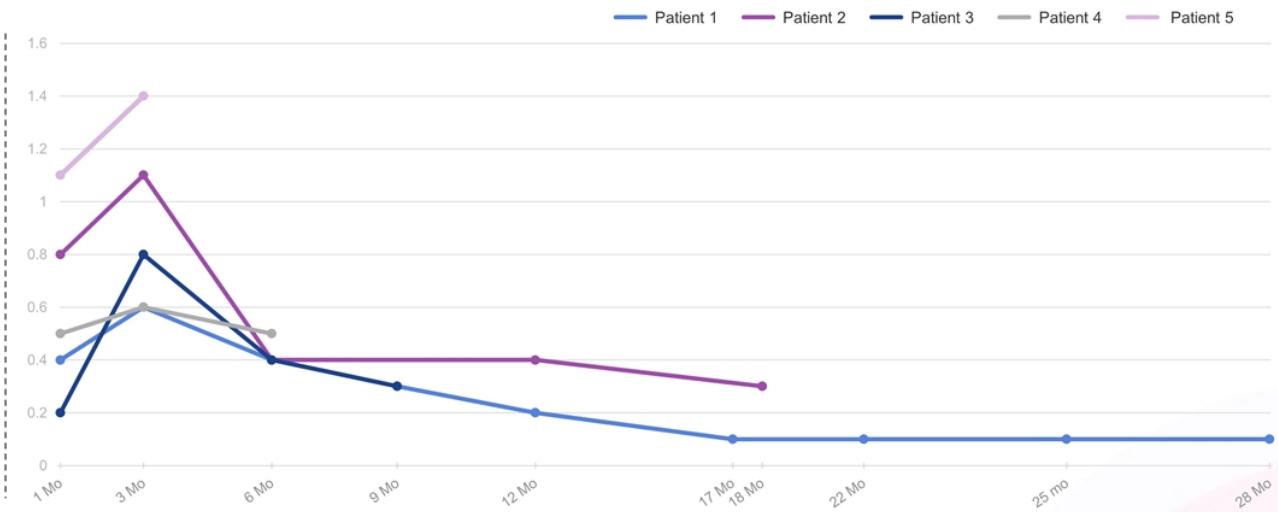
Phase 1: Leukocyte and plasma enzyme activity levels trend consistently across all patients



Note: *Enzyme measurements are taken at ERT troughs; Note: Dotted line illustrative only*
Patient #5's Day 12 data point was utilized since the one month data was not obtained

Phase 1: Consistent VCN trend across all patients

Drug Product VCN	
Patient 1	0.7
Patient 2	1.4
Patient 3	0.8
Patient 4	1.4
Patient 5	1.2



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

Phase 1
5 patients dosed

No unexpected trends or safety events identified

No SAEs related to AVR-RD-01 drug product

AEs and SAEs reported

- **AEs**
  - Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
- **SAEs**
  - Febrile neutropenia (resolved)
  - Thrombophlebitis (resolved)*

Anti-AGA antibodies

- Mild titer rise in 1 patient

Note: *Safety database cut as of May 24, 2019*

**Resolved post-safety database cut-off date*

8 patients
dosed across
2 trials

longest follow-up
>2 years

Emerging data support potential first-line use in Fabry disease

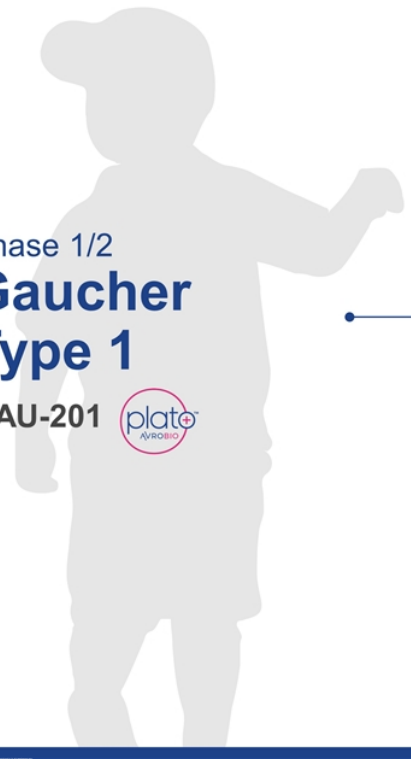
- 87% decrease in Gb3 in first kidney biopsy at 1 year
  in first Phase 2 patient
- Plasma lyso-Gb3 reduced by 30-40% vs. baseline ERT
  in four Phase 1 patients
- Kidney and cardiac function stable at 1 year
  in first Phase 2 patient
- Durability sustained >2 years for enzyme activity and VCN
  in first Phase 1 patient
- No unexpected trends or safety events identified
  8 patients across 2 trials

AVROBIO plato

Steady stream of clinical programs

4 clinical trials up and running

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



Phase 1/2

Gaucher Type 1

GAU-201

- Clinical sites in CA, AUS actively recruiting
- First patient expected to be dosed 2H 2019
- US, CA, AUS manufacturing in place
- Pre-clinical data demonstrates bone improvement

Phase 1/2

Cystinosis

Investigator-Sponsored Trial

- US IND achieved
- Clinical site actively recruiting
- First patient expected to be dosed 2H 2019
- $12M Tier 1 CIRM grant funding to UCSD

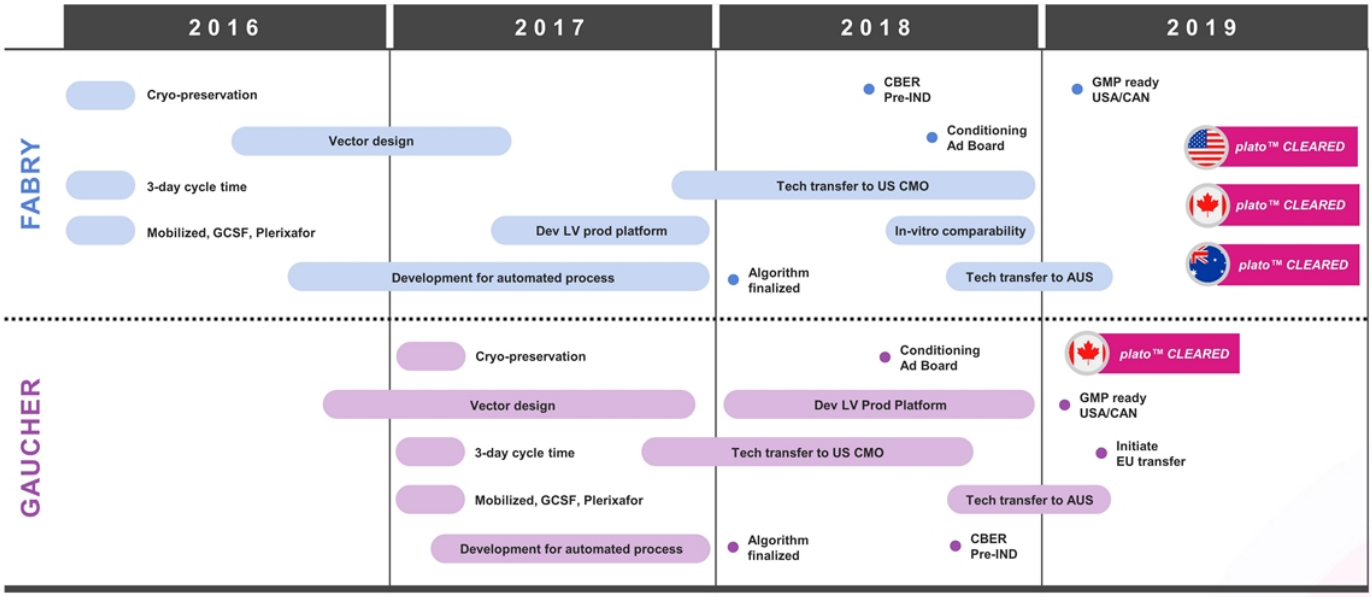
plato™

AVROBIO's foundation for worldwide commercialization

Beginning-to-end manufacturing platform

- **Optimized** for performance
- **Redefines** manufacturing best practices

Multiple plato™ IND and CTA regulatory clearances achieved 1H 2019



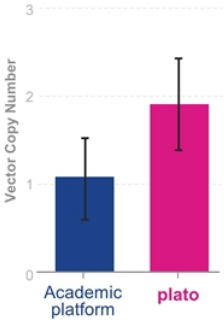
Note: plato in Fabry cleared for use in US via IND, in Canada via protocol and CMC CTA amendment, and in AUS via CTN and HREC clearance; plato in Gaucher cleared for use in Canada via CTA and protocol CTA amendment

plato™ optimized for performance

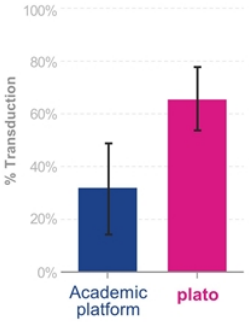
Proprietary Vector Toolbox

- OPTIMIZED VECTOR
- PROMOTERS
- OPTIMIZED TRANSCRIPTION
- OPTIMIZED TRANSLATION
- TAGS
- KOZAK SEQUENCE
- CODON OPTIMIZATION

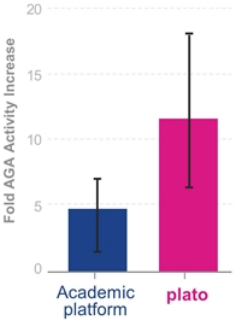
VCN



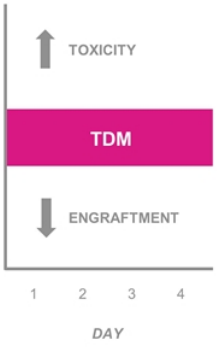
Transduction Efficiency



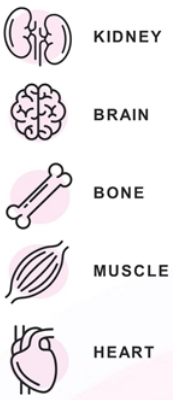
Enzyme Activity



Therapeutic Drug Monitored (TDM) Conditioning

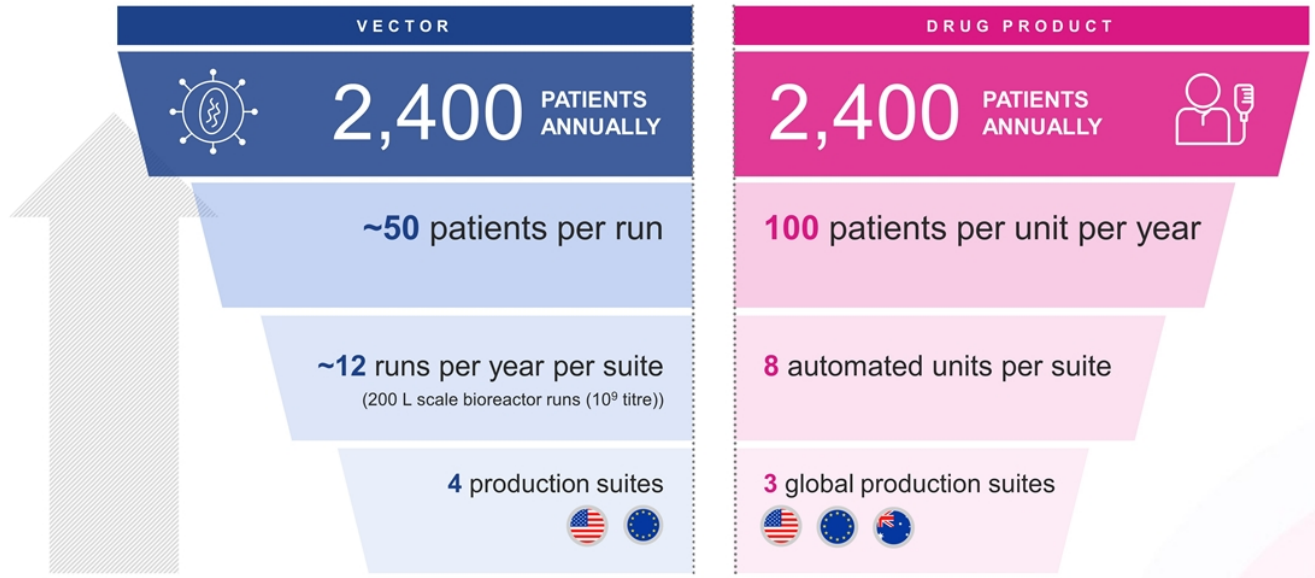


Distribution



Note: Data from appropriate runs from normal donors and patients are included in the analysis; Data cutoff March 12, 2019

plato™ platform designed to be scalable for commercial supply

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Multiple 2H 2019 milestones anticipated

FABRY

- Continued recruitment in FAB-201, with plato™ to be incorporated
- FAB-201 clinical sites to expand into USA and Canada

GAUCHER

- Dose first patient in GAU-201, incorporating plato™ from the outset

CYSTINOSIS

- Dose first patient in investigator-sponsored trial

POMPE

- Pre-clinical IND-enabling study to be initiated

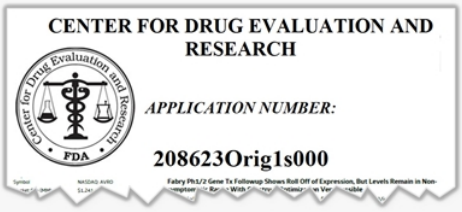
Key take-aways for today

- 87% substrate reduction in first kidney biopsy, an endpoint used by FDA and EMA
  in first Phase 2 patient
- Toxic metabolite levels of patients treated with AVR-RD-01 are 30-40% below baseline ERT levels
  in first four Phase 1 patients
- Durability of AVR-RD-01 sustained >2 years and stable across multiple measures
  in first Phase 1 patient
- On track to achieve goal of 3 investigational gene therapies in the clinic 2H 2019
- Commercially scalable plato™ platform in place

Appendix

Precedent for use of kidney biopsy data for FDA approval of drug candidate for Fabry disease

Migalastat approved on % reduction in GL-3 inclusions per KIC as compared to placebo



CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208623Orig1s000

Fabry Ph1/2 Gene Tx Followup Shows Roll Off of Expression, But Levels Remain in Non-

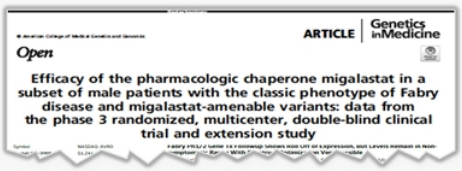
45 Amenable patients* (16 males / 29 females)

Group	Migalastat (BL –M6)	Placebo (BL –M6)
Males (N=16)	5/7 (71%) -1.10 (-1.94, -0.02)	4/9 (44%) -0.03 (-1.00, 1.69)
Patients with baseline GL-3 ≥ 0.3 (N=17; 9 males, 8 females)	7/9 (78%) -0.91 (-1.94, 0.19)	2/8 (25%) -0.02 (-1.00, 1.69)
Patients with baseline GL-3 < 0.3 (N=28; 7 males, 21 females)	6/16 (38%) -0.02 (-0.10, 0.26)	7/12 (58%) -0.05 (-0.16, 0.14)

7/9 males ≥ 50% reduction
(at 6 months from baseline)

Treatment Group	n	Baseline Median (min, max)	Month 6 Median (min, max)	Change from Baseline Median (min, max)
Average number of GL-3 inclusions per KIC (N=13)				
Galafold	7	3.6 (0.2, 6.0)	2.6 (0.1, 6.0)	-0.7 (-1.7, 1.2)
Placebo	6	1.8 (0.1, 2.8)	2.0 (0.05, 4.3)	-0.04 (-0.5, 1.5)

28% average reduction
(at 6 months from baseline)



ARTICLE | Genetics in Medicine

Open

Efficacy of the pharmacologic chaperone migalastat in a subset of male patients with the classic phenotype of Fabry disease and migalastat-amenable variants: data from the phase 3 randomized, multicenter, double-blind clinical trial and extension study

Fabry Ph1/2 Gene Tx Followup Shows Roll Off of Expression, but Levels Remain in Non-

Source: *Germain D et al, Genetics in Medicine, 2019*

Classic Fabry patient level data

0-6 months randomized clinical trial and 6-12 months open label extension

	Male Patients with the Classic Phenotype													
	Migalastat (Months 0-24)							Placebo (Months 0-6) → Migalastat (Months 6-24)						
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14
PTC GL-3 inclusions at BL	0.16	0.03	n/a	5.69	1.22	n/a	2.88	2.41	1.55	0.16	0.03	0.11	0.94	0.88
Change in PTC GL-3 inclusions from BL to M6	-0.08	0.01	n/a	-1.77	-1.10	n/a	-1.25	1.21	-0.21	0.01	0.09	-0.07	1.94	-0.83
Change in PTC GL-3 inclusions from BL/M6[b] to M12	-0.12	n/a	n/a	-1.92	n/a	n/a	-0.81	-0.94	-1.13	-0.09	-0.05	n/a	-2.28	0.06

46% average reduction
(average of patients with 12 month data)

- *Classic Fabry disease (AGA activity <1%)*
- ***NOTE:*** *For informational purposes; differences exist between trial designs and subject populations; AVROBIO has not conducted any head-to-head trials comparing migalastat to AVR-RD-01*