AVROBIO

Company Presentation

Wedbush PacGrow Healthcare Virtual Conference

August 2020

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Any forward-looking statements in this presentation are based on our current expectations, estimates and projections about our industry as well as management's current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of our product candidates will not be successfully developed or commercialized; the risk of cessation or delay of any ongoing or planned clinical trials of AVROBIO or our collaborators; the risk that we may not successfully recruit or enroll a sufficient number of patients for our clinical trials; the risk that we may not realize the intended benefits of our gene therapy platform, including the features of our plato platform; the risk that our product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that we anticipate; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical or clinical trials, will not be replicated or will not continue in ongoing or future studies or trials involving our product candidates; the risk that we will be unable to obtain and maintain regulatory approval for our product candidates; the risk that the size and growth potential of the market for our product candidates will not materialize as expected; risks associated with our dependence on third-party suppliers and manufacturers; risks regarding the accuracy of our estimates of expenses and future revenue; risks relating to our capital requirements and needs for additional financing; risks relating to clinical trial and business interruptions resulting from the 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 from those contained in the forward-looking statements, see the section entitled "Risk Factors" in AVROBIO's most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties and other important factors in AVROBIO's subsequent filings with the Securities and Exchange Commission. AVROBIO explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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AVROBIO
Our mission: Giving people with genetic disease freedom for life

Established *ex vivo* lentiviral approach

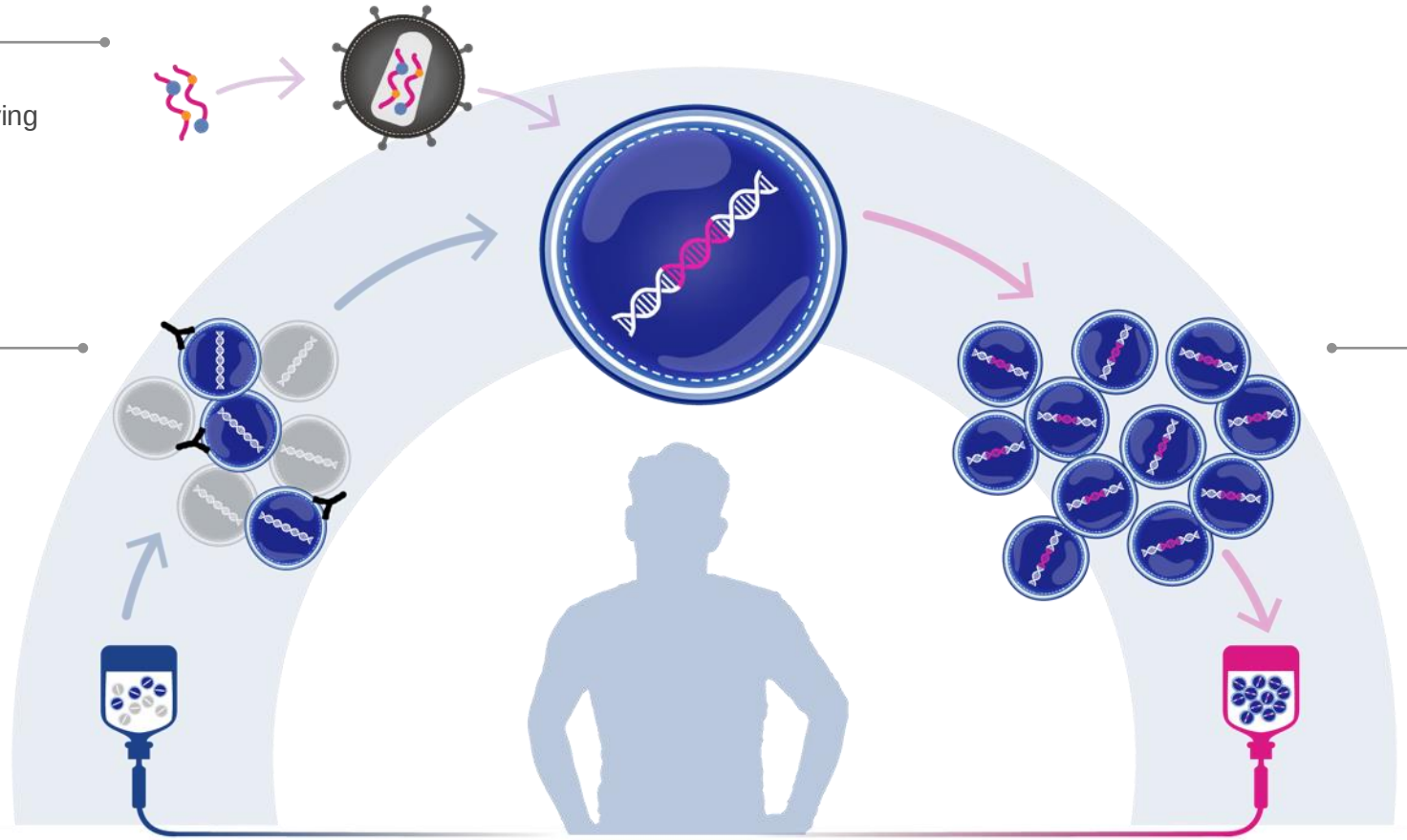
3 **Transduce** with lentiviral vector carrying therapeutic gene

2 **Select** CD34+ stem cells

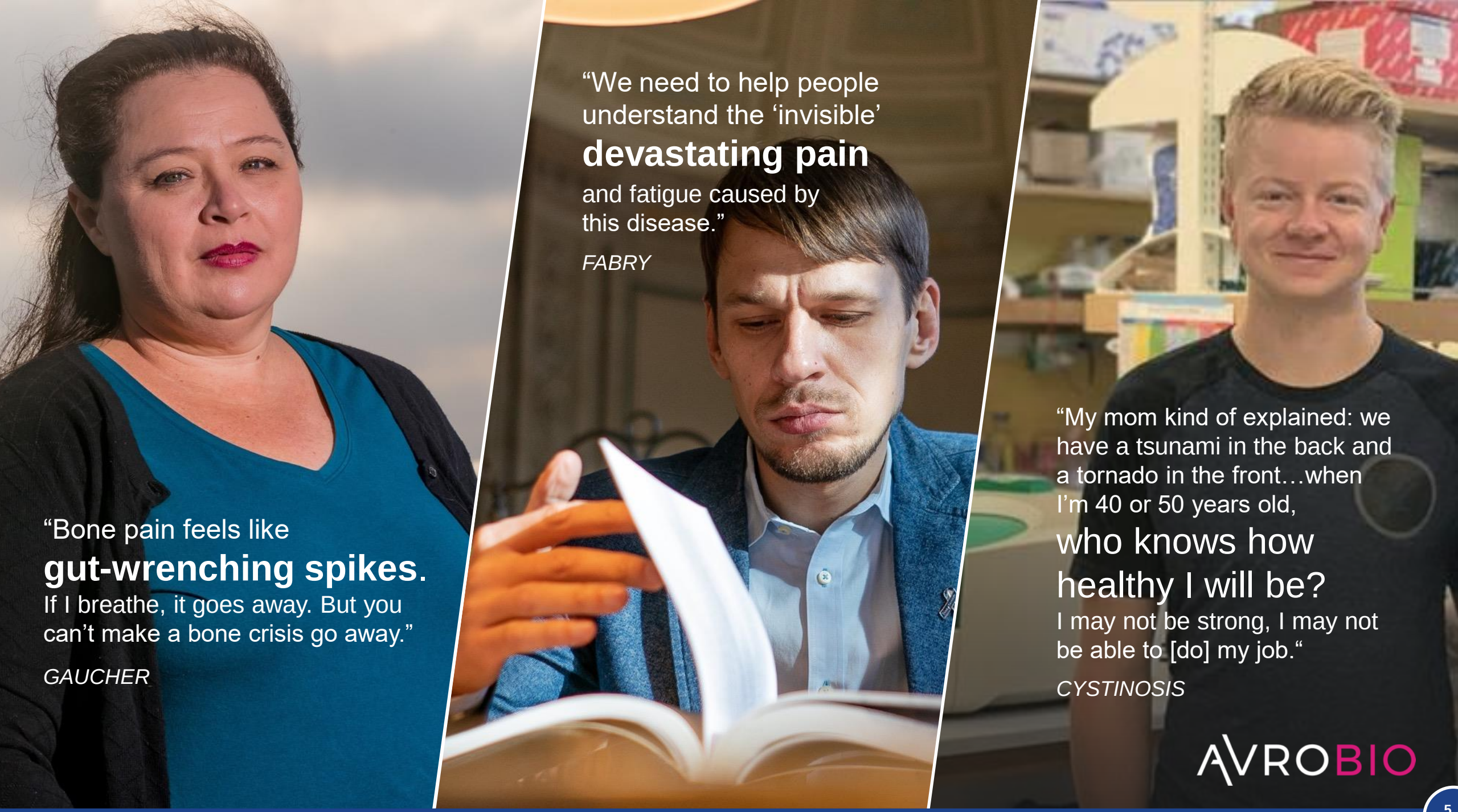
1 **Collect** mobilized blood

Harvest and freeze **4**

Condition and dose **5**



GENE THERAPY APPROACH


“Bone pain feels like
gut-wrenching spikes.
If I breathe, it goes away. But you can’t make a bone crisis go away.”
GAUCHER
“We need to help people understand the ‘invisible’
devastating pain
and fatigue caused by this disease.”
FABRY
“My mom kind of explained: we have a tsunami in the back and a tornado in the front…when I’m 40 or 50 years old,
who knows how healthy I will be?
I may not be strong, I may not be able to [do] my job.“
CYSTINOSIS
AVROBIO

Multiple programs in the clinic

12 patients dosed to date across **three indications**

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

Addressing multi-billion dollar market opportunity

CURRENT STANDARD OF CARE COSTS

Disease	Est. Cost Per Patient Per Year	Approx. 2019 Net Sales	Selected Companies
Fabry	$320k	$1.4B	SANOFI GENZYME, Takeda Shire
Gaucher	$250k-400k	$1.4B	SANOFI GENZYME, Takeda Shire
Pompe	$500k	$1.0B	SANOFI GENZYME
Cystinosis	$625k-700k*	$0.2B	HORIZON PHARMA, Mylan, RECORDATI

Sources: Rombach S et al, Orphanet J Rare Dis, 2013; van Dussen L et al, Orphanet J Rare Dis, 2014; WAC pricing from Redbook; 2019 Net Sales from company annual and other reports
** for Horizon's Procysbi oral therapy (delayed release cysteamine bitartrate)*
Note: Shire acquired by Takeda in 2019

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

Sources: Wanner C et al, Med Genetics and Metab, 2018; Burlina A, JIEMS, 2016
CNS: Central Nervous System; TIA: Transient Ischemic Attack

Two AVR-RD-01 Fabry clinical trials

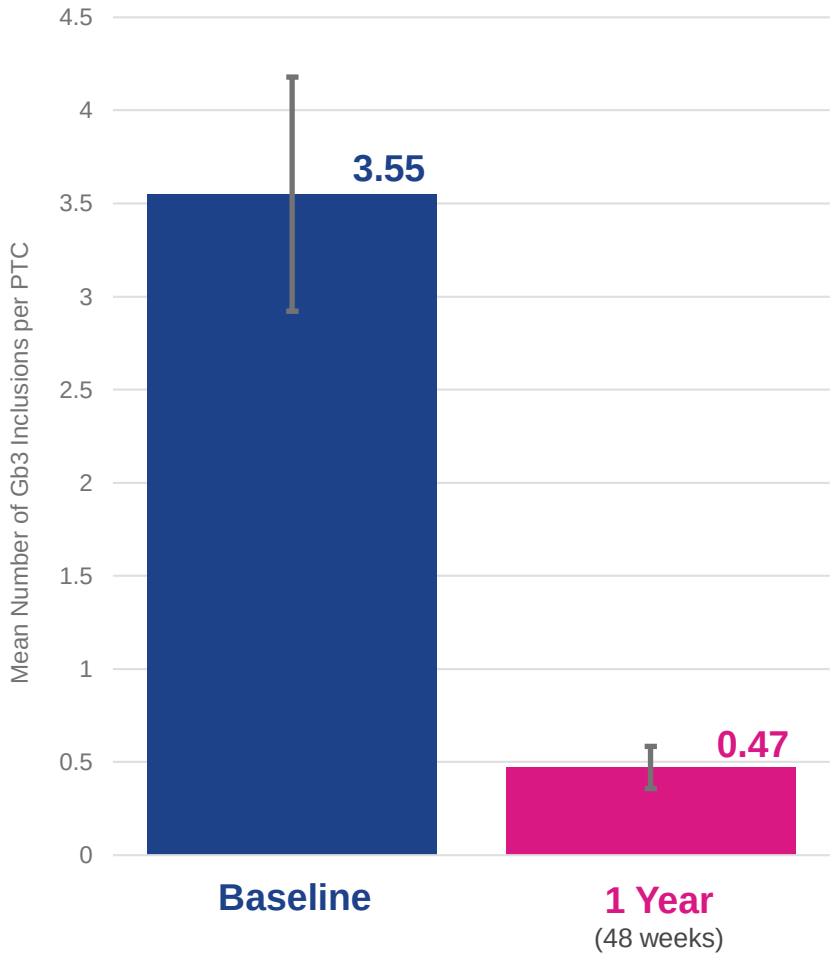
9 patients dosed across Phases 1 and 2

PHASE 1 Investigator-Sponsored Trial*	PHASE 2 AVRO – FAB-201 Trial
Patients **n = 5 (fully enrolled)** **On ERT > 6 months prior to enrollment** **18 - 50 year-old males**	**Patients** **n = 8-12 (4 patients dosed to-date)** **Treatment-naive** **16 - 50 year-old males**
Key Objective Safety and preliminary efficacy	**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

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

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



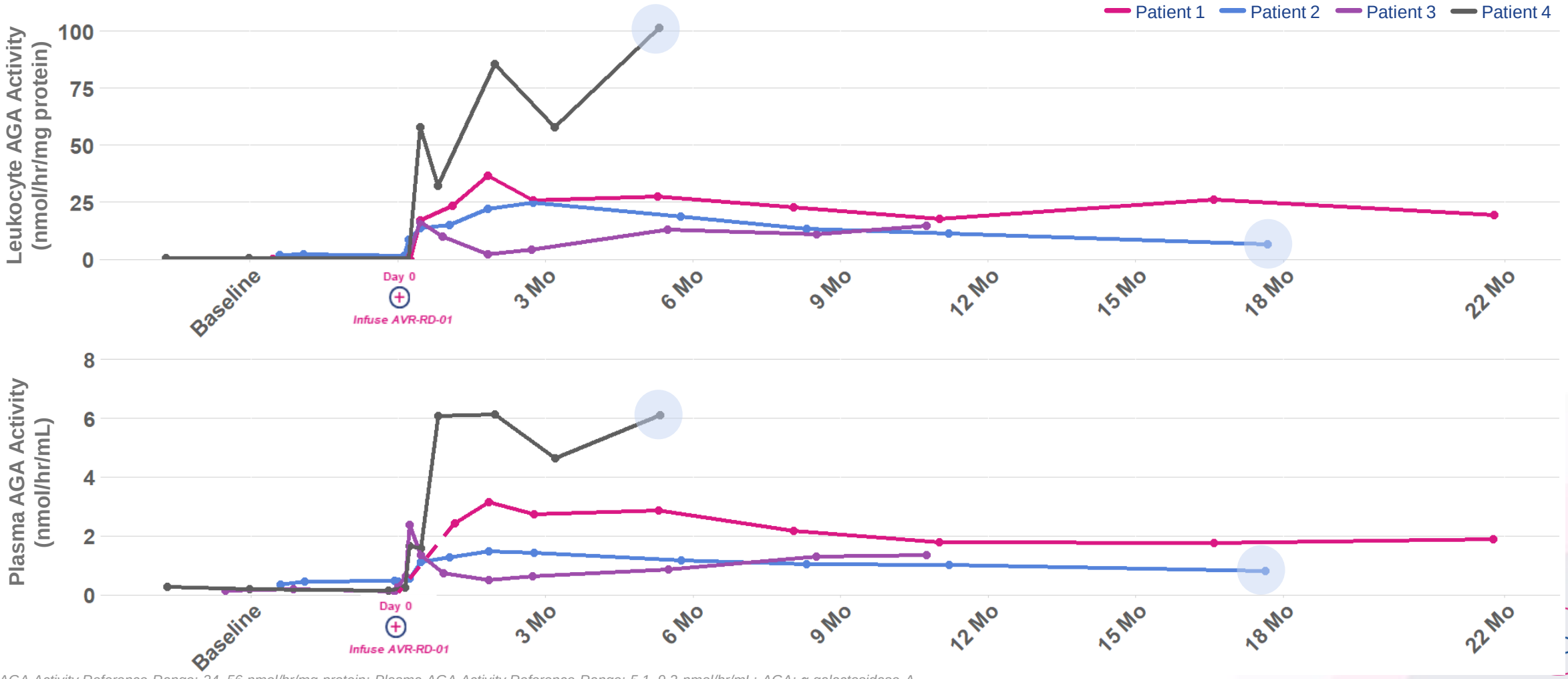
- *Unpaired t-test for difference between n=55 PTCs at baseline vs. n=101 PTCs at 1 year; p < 0.0001*
- *Error bar represents the standard deviation*

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 data point

Patients 1-4: Leukocyte and plasma enzyme activity sustained up to 22 months

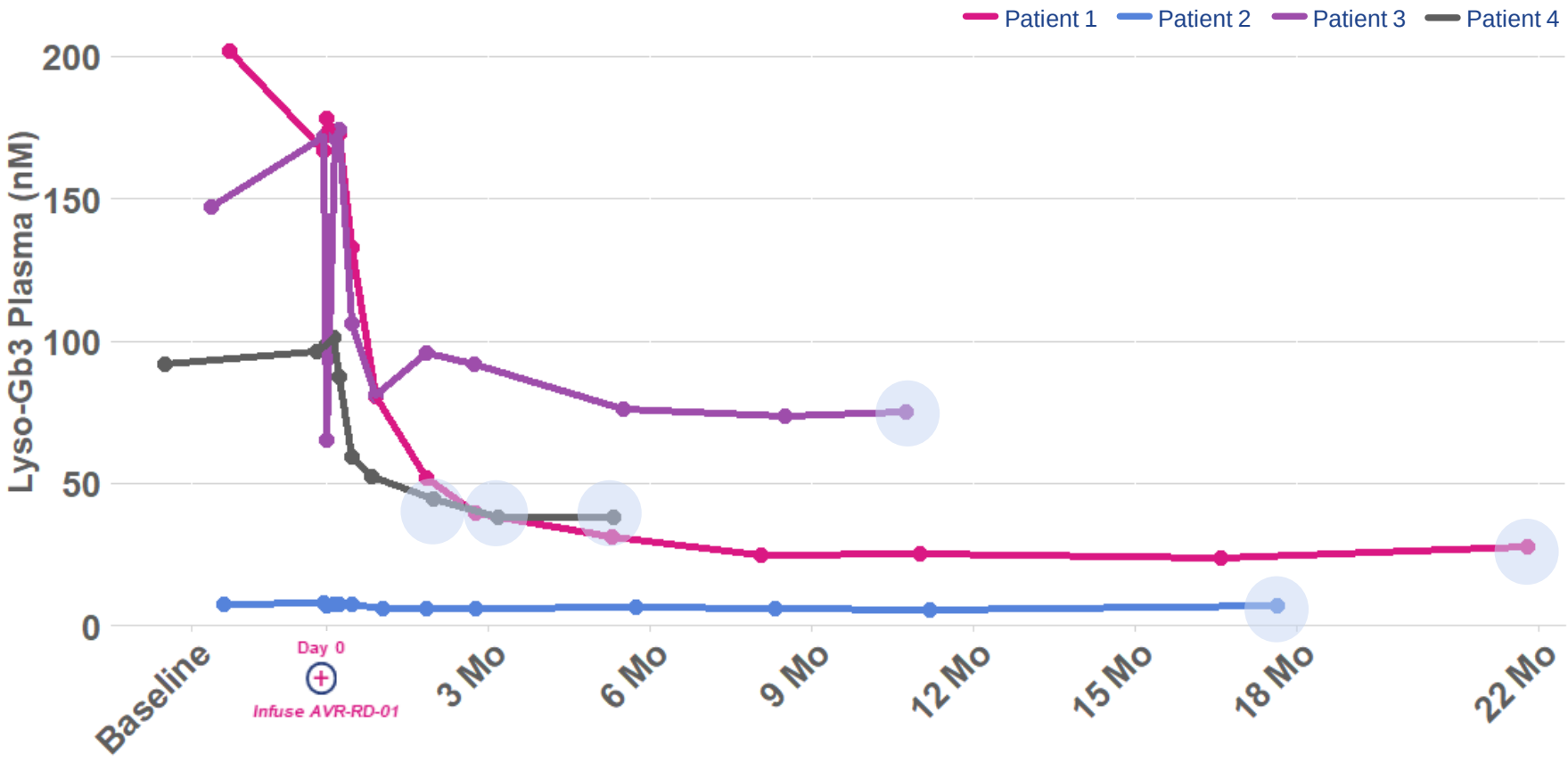
Patient #4 dosed using plato®



Leukocyte AGA Activity Reference Range: 24–56 nmol/hr/mg protein; Plasma AGA Activity Reference Range: 5.1–9.2 nmol/hr/mL; AGA: α-galactosidase A

New data point

Patients 1-4: Plasma lyso-Gb3 reduction sustained up to 22 months



Reduction from Baseline to Last Observation	
Patient 1	86%
Patient 2	NA
Patient 3	49%
Patient 4	59%

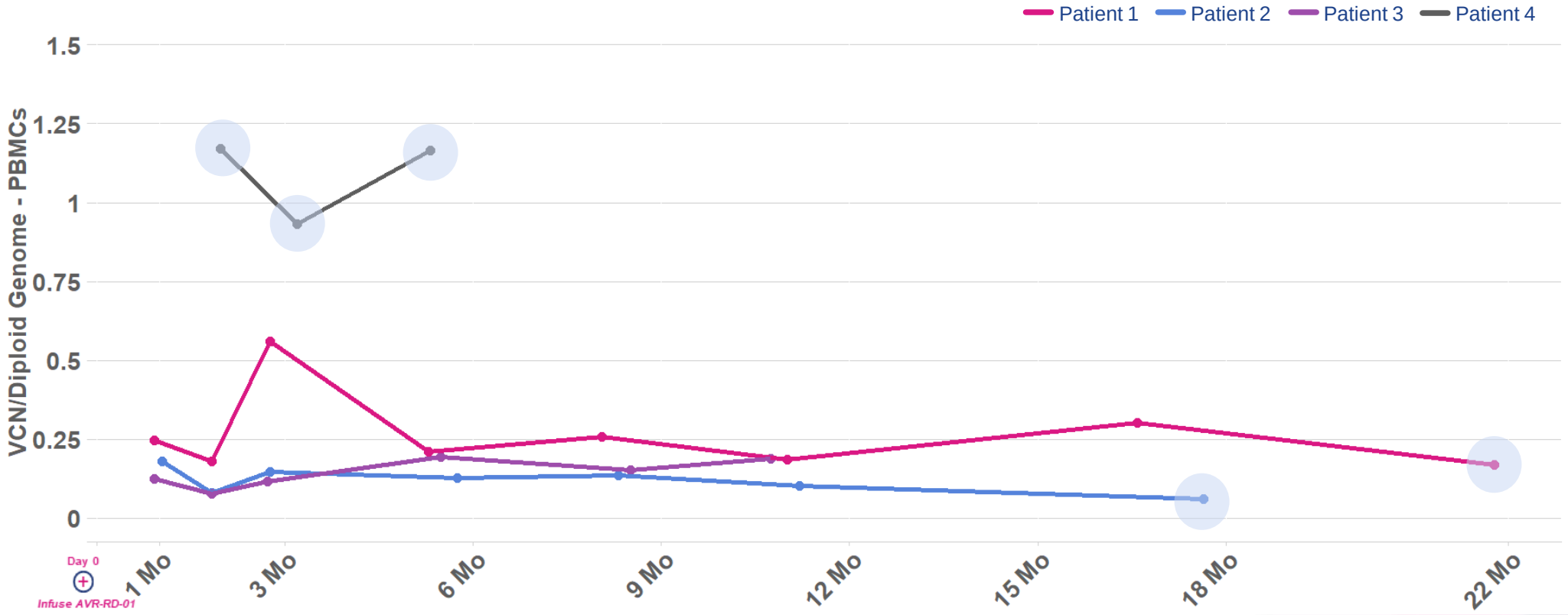
- *Lyso-Gb3 Plasma Reference Value: 2.4 nM; Lyso-Gb3: Globotriaosylsphingosine*
- *Note: Patient #2 has normal substrate, consistent with late-onset cardiac variant phenotype*

New data point

Patients 1-4: VCN stable up to 22 months

Patient #4 dosed using plato®

Drug Product VCN/dg	
Patient 1	0.7
Patient 2	0.5
Patient 3	1.4
Patient 4	1.6



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

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

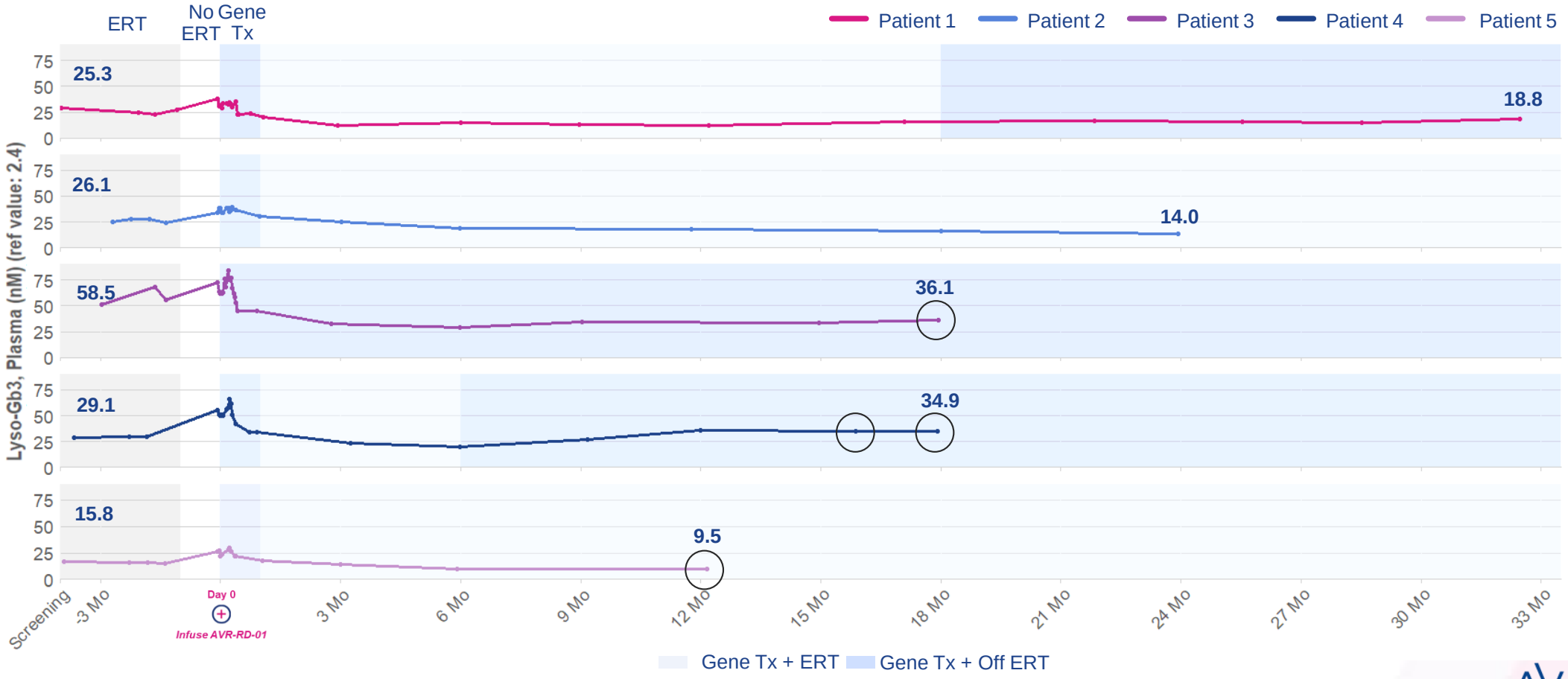
Safety and efficacy

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

New data point

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

All patients who have discontinued ERT remain off ERT*



26% reduction *from baseline ERT* **OFF ERT**

47% reduction *from baseline ERT* **ON ERT**

38% reduction *from baseline ERT* **OFF ERT**

20% increase *from baseline ERT* **OFF ERT**

40% reduction *from baseline ERT* **ON ERT**

** As of July 21, 2020*

Lyso-Gb3 Plasma Reference Value: 2.4 nM; Lyso-Gb3: Globotriaosylsphingosine; ERT: Enzyme Replacement Therapy; Tx: Therapy

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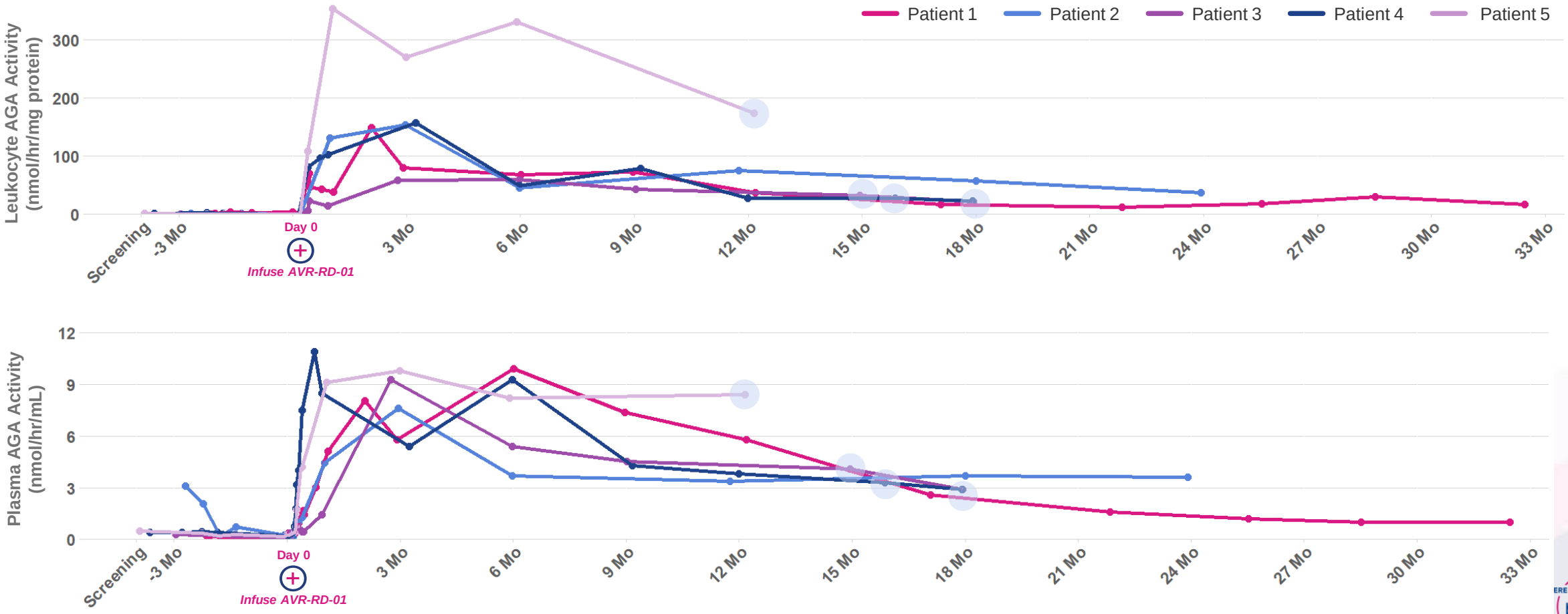
New data point

Leukocyte and plasma enzyme activity sustained up to 32 months with consistent trend across all other patients

All 5 patients now out 1 year or more



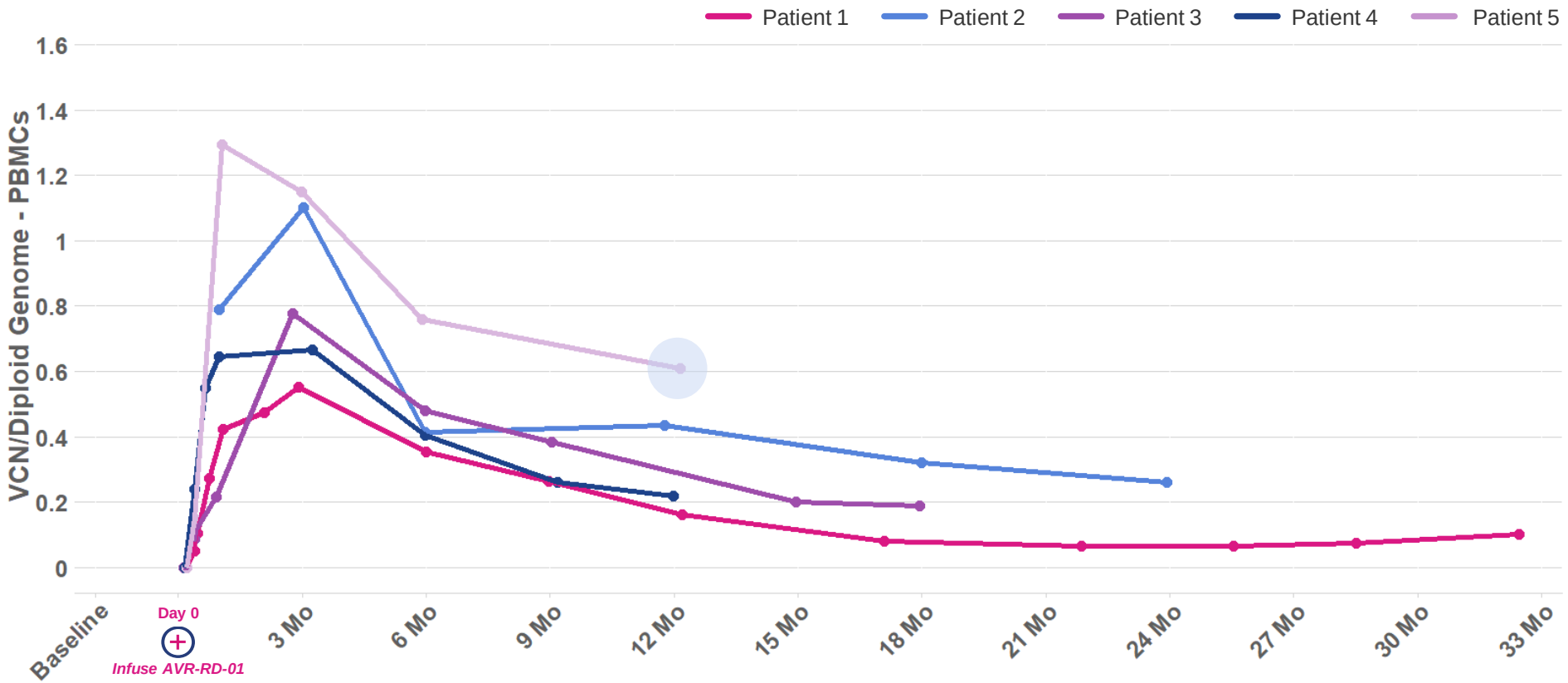
Leukocyte AGA Activity Reference Range: 24–56 nmol/hr/mg protein; Plasma AGA Activity Reference Range: 5.1–9.2 nmol/hr/mL; AGA: α-galactosidase A

New data point

Patients 1-5: VCN stable at 32 months with consistent trend across all other patients

All 5 patients now out 1 year or more

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

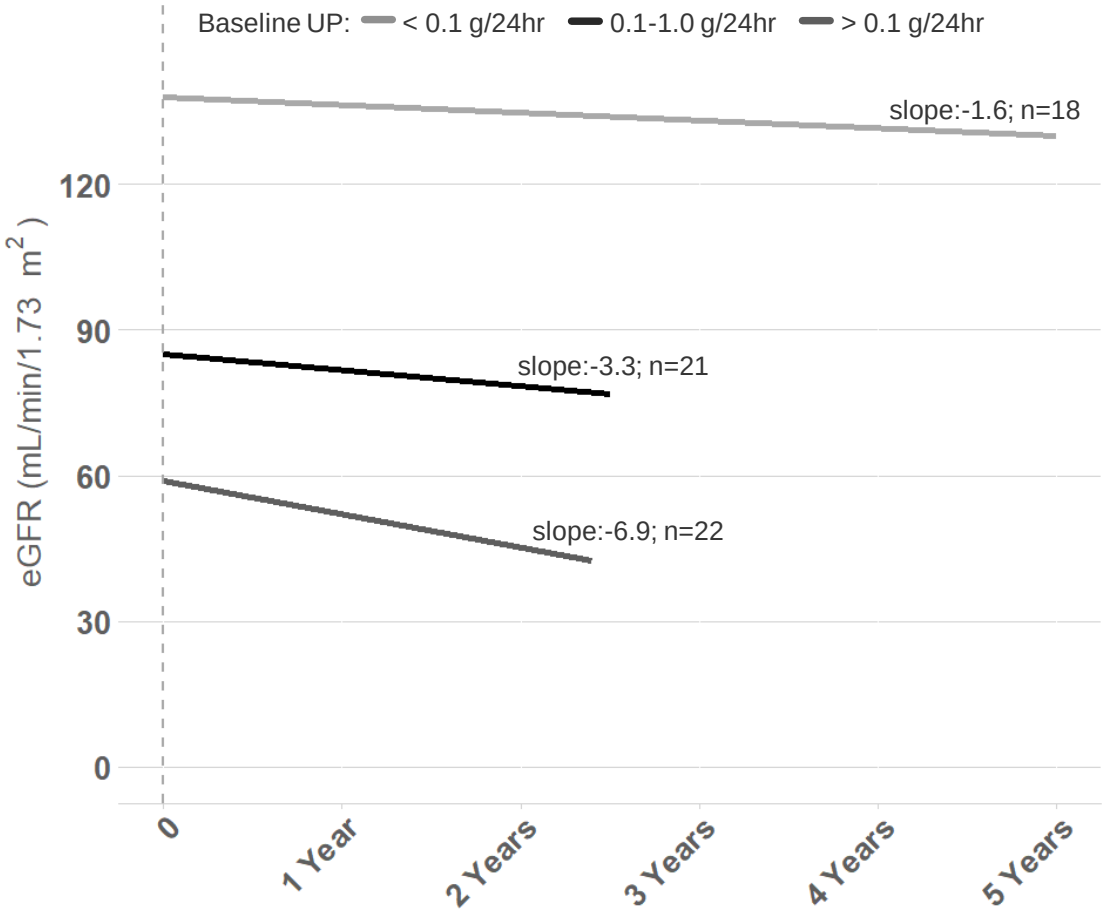


Note: 0.1 VCN is indicative of approx. 5-10% of all nucleated cells having an average of 1-2 copies of the transgene
VCN: Vector Copy Number

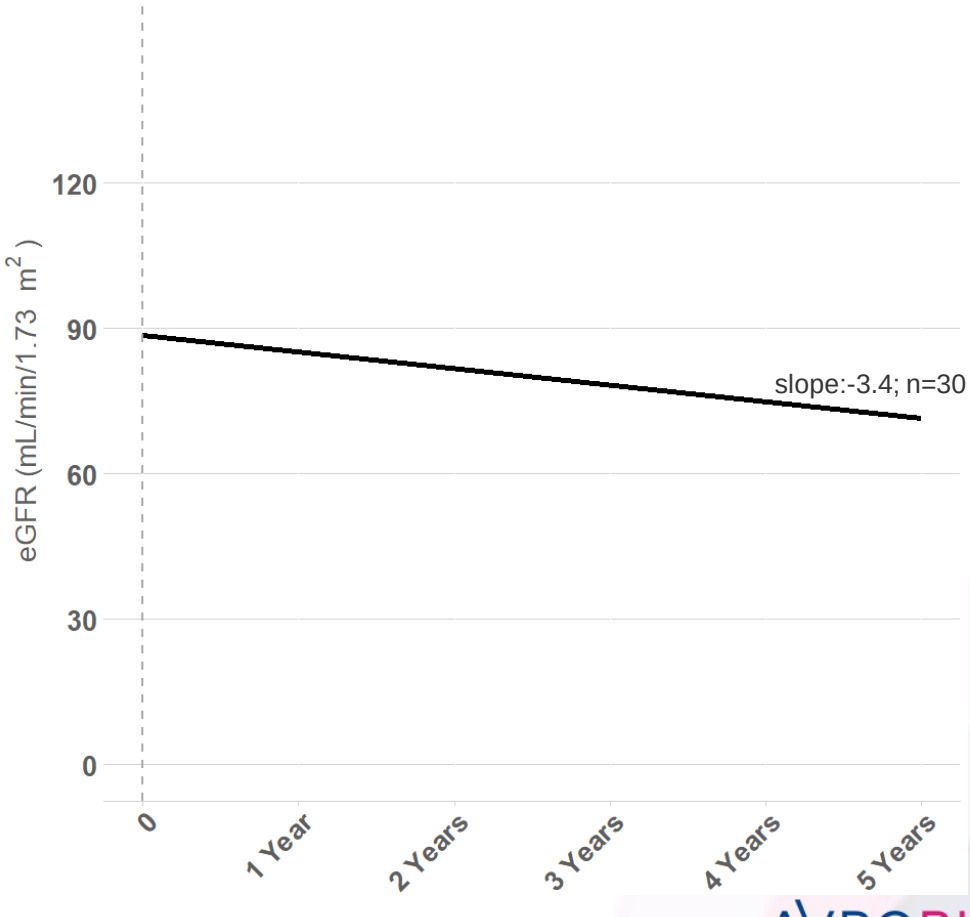
eGFR declines in natural history and on ERT

Classic Fabry male literature eGFR data

Natural history annualized eGFR slopes of treatment naïve patients*



Annualized eGFR slope of ERT-treated patients**

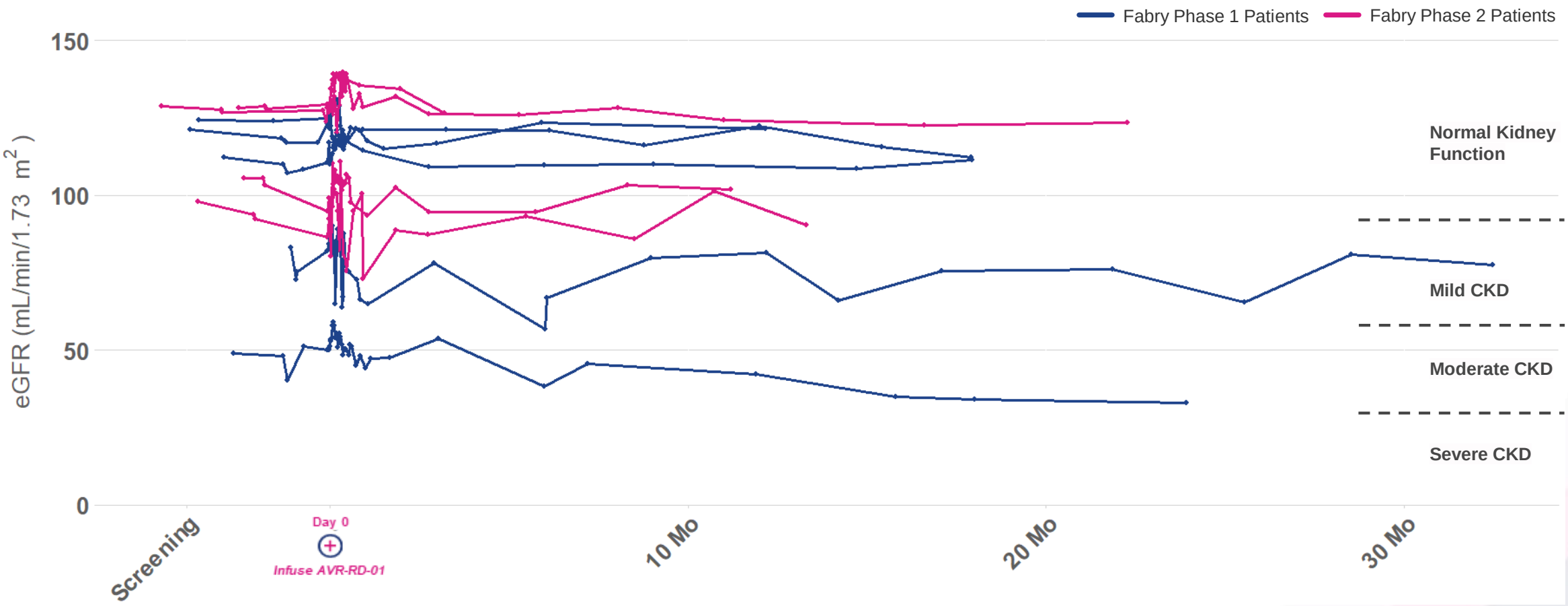


eGFR: Estimated Glomerular Filtration Rate; UP: Urinary Protein

*Sources: *Schiffmann R et al, Nephrol Dial Transplant, 2009 (Table 4); ** Rombach SM et al, Orphanet J Rare Dis 2013 (Table 2)*

New data points

Kidney function stable across Phase 1 and Phase 2 trials, up to 32 months*



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

eGFR: Estimated Glomerular Filtration Rate

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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 = 100):

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

FAB 201 AEs (n = 91):

- Generally consistent with myeloablative conditioning, underlying disease or pre-existing conditions
  - Grade 1 or 2 (n = 74)
  - Grade 3 or 4 (n = 17)

Phase 1 SAEs (n = 2):

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

FAB 201 SAEs: (n = 6)

Pre-treatment and prior to conditioning

- Seizure (grade 2)

Post-treatment

- Dehydration, nausea, vomiting (grade 3)
- Febrile neutropenia (2 patients, grade 3 & 4)
- Culture negative fevers (grade 2)
- Mucositis (grade 2)

Anti-AGA antibodies

- Anti-AGA antibody titers observed in 4 patients in the Phase 1 trial and 2 patients in FAB-201. We believe none of these are of clinical significance.

Note: Safety data cut off April 23, 2020
AE: Adverse Event; SAE: Serious Adverse Event
NOTE: AVR-RD-01 is an investigational gene therapy

Building commercial capabilities

44+ product launches, including 1 gene therapy

Holly May
Chief Commercial Officer

- Led commercial teams for LSDs at SanofiGenzyme
- Head of Commercial at SOBI, a rare disease company

SANOFI GENZYME

sobi
Pioneer in Rare Diseases

Jose Gomez
SVP, Global Market Access & Value

- Led global strategic marketing and global market access functions at AveXis
- Led market access, global strategic pricing and reimbursement functions for LSDs at Shire

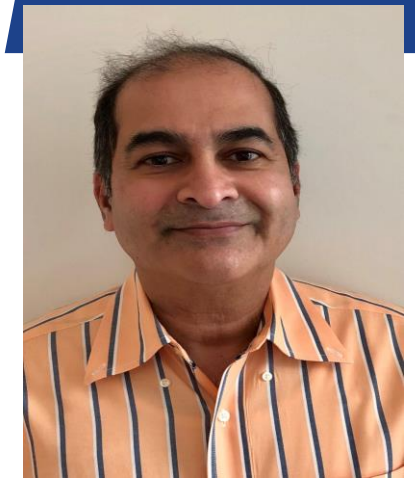
Shire avexis

Sean Ring
VP, Head of Commercial Operations

- Extensive orphan drug commercial strategy and launch expertise
- Built out market development and commercial ops at Editas, Zafgen, Cubist, Shire, Biogen

Shire editas MEDICINE

Ramesh Arjunji
VP, Global Health Economics and Outcomes Research / Value Demonstration



- Led value demonstration for insurers globally at AveXis
- Significant access and reimbursement responsibilities at leading global biotech companies

avexis Biogen

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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

Two patients 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

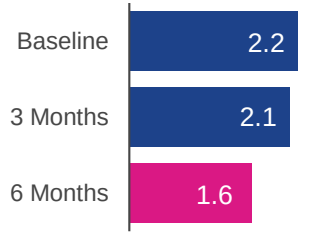
** Sponsored by University of California, San Diego*
Note: AVR-RD-04 aka CTNS-RD-04

Patient 1: Initial data indicate positive trends across multiple measures

CLINICAL LAB MEASURES

Kidney Function

eGFR (mL/min/1.73m²)
normal range: >90



Serum Creatinine (mg/dL)
normal range: 0.7-1.2

Urine Volume
24 Hour Urine Volume in L

BIOMARKER ENDPOINTS

Levels of Cystine in Skin*
µm³

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

VCN
(vcn/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: Cystinosin, 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*

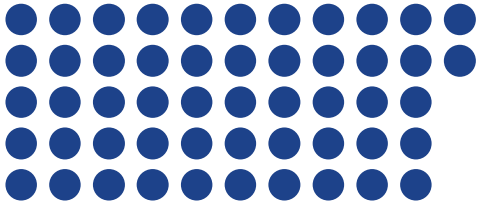
Patient 1: Reduced treatment burden at 6 months

Number of Medications and Supplements

(max per day)

Before Gene Therapy

ON Cysteamine



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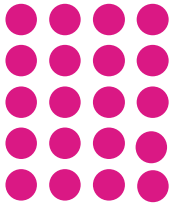
After Gene Therapy

(at 6 months post-gene therapy)

OFF Cysteamine



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NOTE: Investigational gene therapy

Phase 1/2 Cystinosis

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 for first patient dosed in the trial
AE: Adverse Event; SAE: Serious Adverse Event

Gaucher Disease

AVR-RD-02

Goals for gene therapy in **Gaucher Type 1 Disease**

UNMET NEEDS:

Bone-related manifestations
Unmet needs: bone pain, avascular necrosis, bone crisis, osteoporosis, fractures, joint destruction, skeletal abnormalities

Hemoglobin levels and platelet counts
Unmet needs: anemia, thrombocytopenia, easy bruising, bleeding

Hepatosplenomegaly
Unmet needs: enlarged liver, enlarged spleen

CNS complications
Unmet needs: Increased risk of GBA-Parkinson's disease

Everyday burden of illness, and life expectancy
Unmet needs: fatigue, pain, lung disease, biweekly infusions, shortened lifespan

Sources: Grabowski G et al, Online Metabolic and Molecular Bases of Inherited Disease, 2018; Weinreb N et al, AJH, 2008; Pastores G et al, Semin Hematol, 2004
CNS: Central Nervous System; GBA: gene coding for glucocerebrosidase

GuardOne: Phase 1/2 study in Gaucher Type 1 patients

First patient dosed

PHASE 1/2
AVR-RD-02 Trial

Patients

n = 8 - 16
Type 1 Gaucher
Treatment naïve or on ERT
16 - 35 year-old
Male and Female

Key Objectives

Safety, Engraftment, Efficacy, ERT-independence

GAU-201: AVR-RD-02 Study; ERT: Enzyme Replacement Therapy

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

POWERED BY AVROBIO 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)

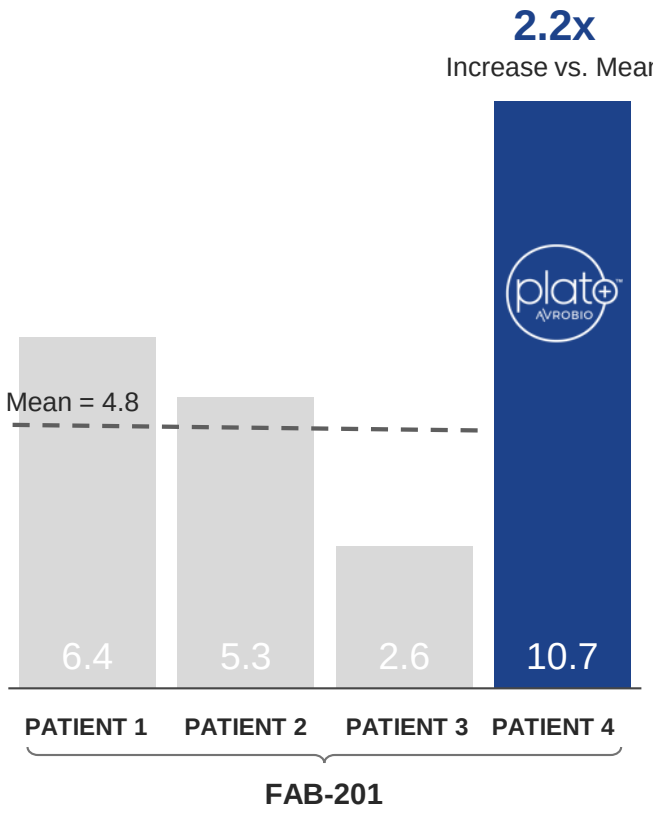
plato® UPGRADE 1

VECTOR UPGRADE:

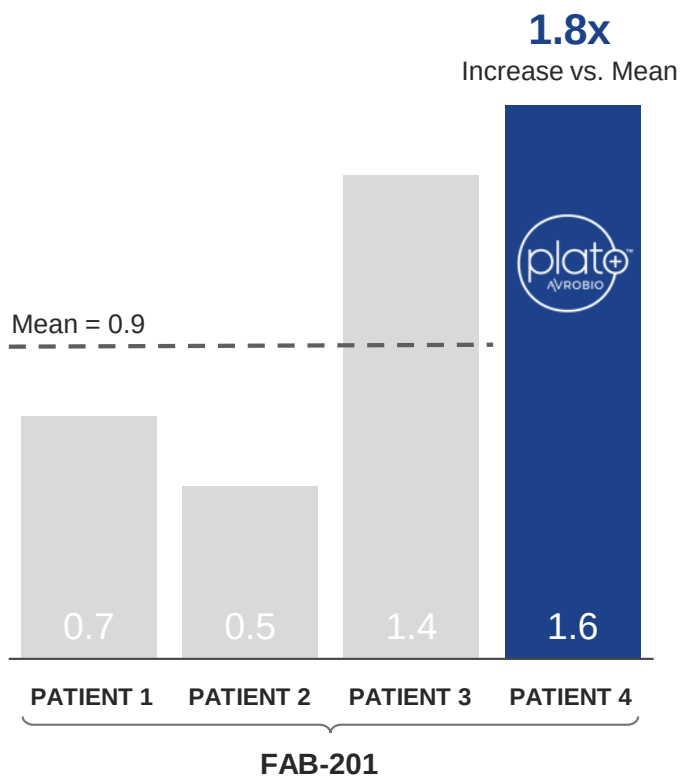
Metrics compared to academic process

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

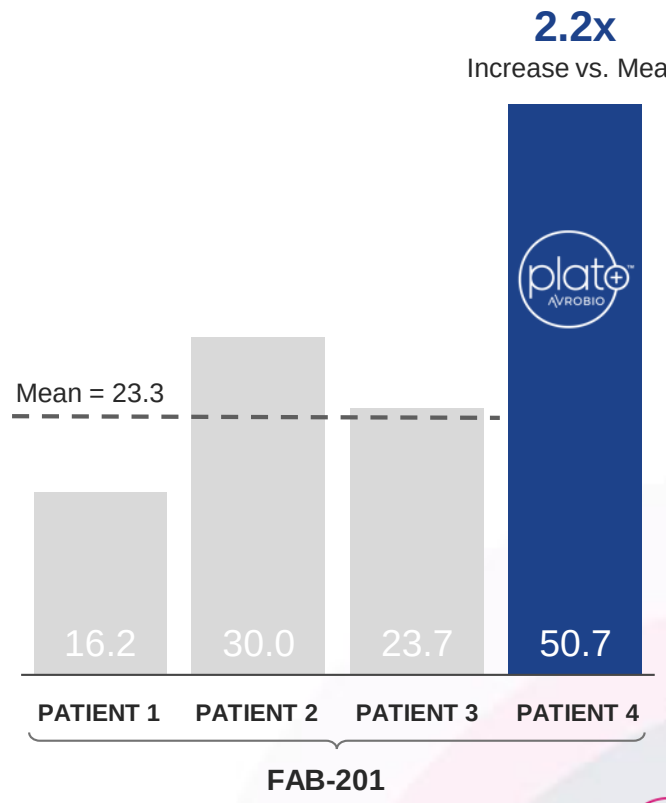
Enzyme Activity (nmol/hr/mL)



VCN (per diploid genome)



Transduction Efficiency (%)



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

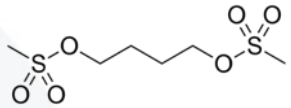
POWERED BY AVROBIO plato

plato®
UPGRADE
2

PRECISION CONDITIONING UPGRADE:

Designed to access “hard-to-reach” compartments

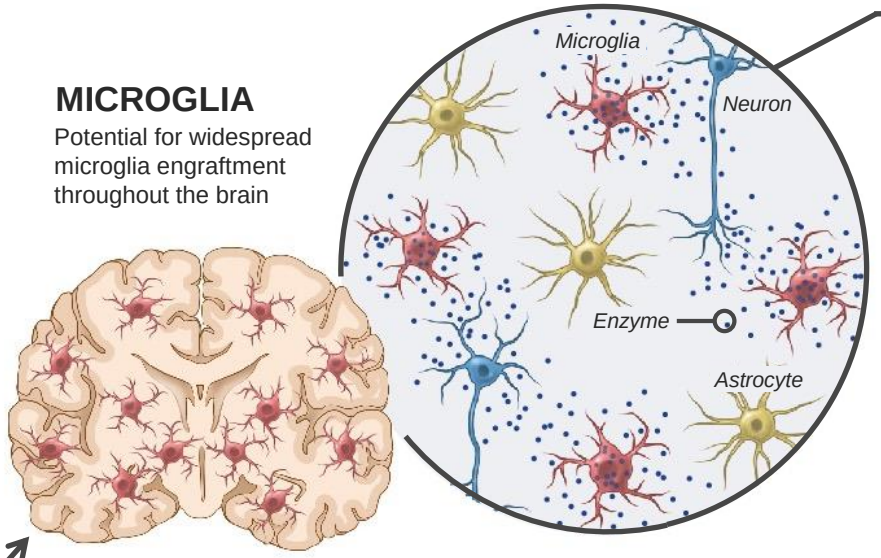
BRAIN
Busulfan crosses blood-brain barrier and eliminates resident microglia cells making space for gene-modified cells



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

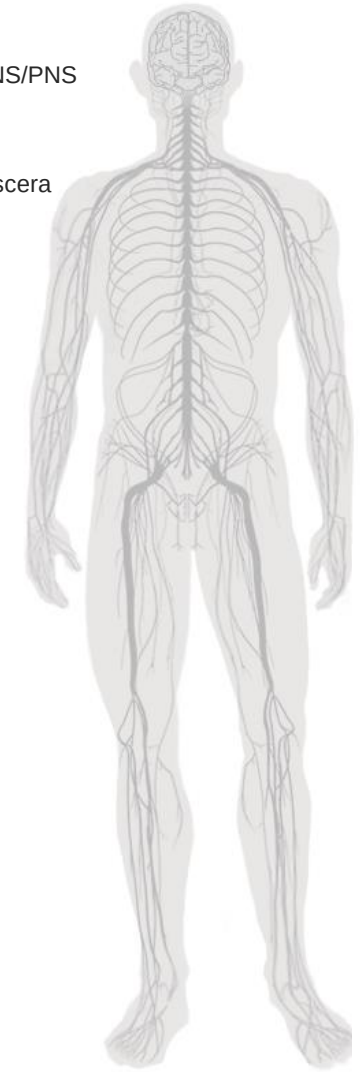
TRANSDUCED CD34+ CELLS

MICROGLIA
Potential for widespread microglia engraftment throughout the brain

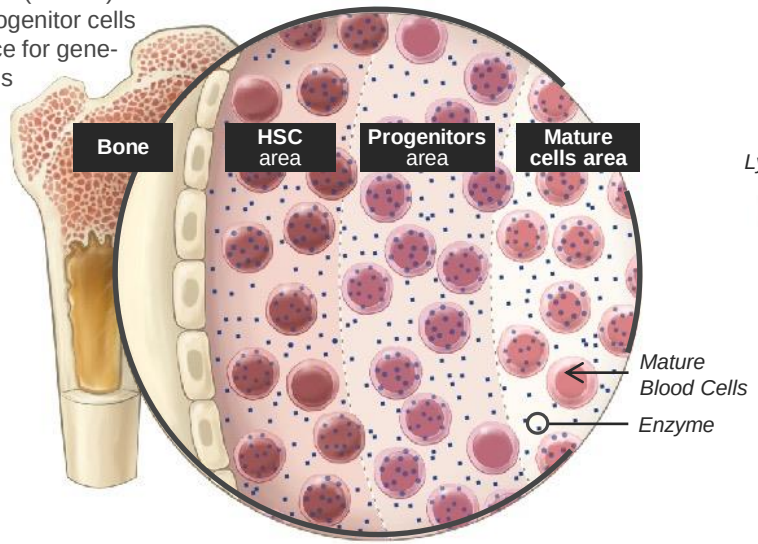


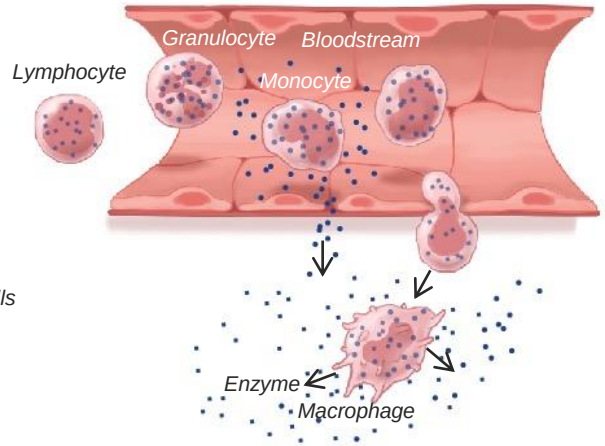
CNS/PNS

Viscera



BONE MARROW → PERIPHERAL TISSUE





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plato® UPGRADE 2

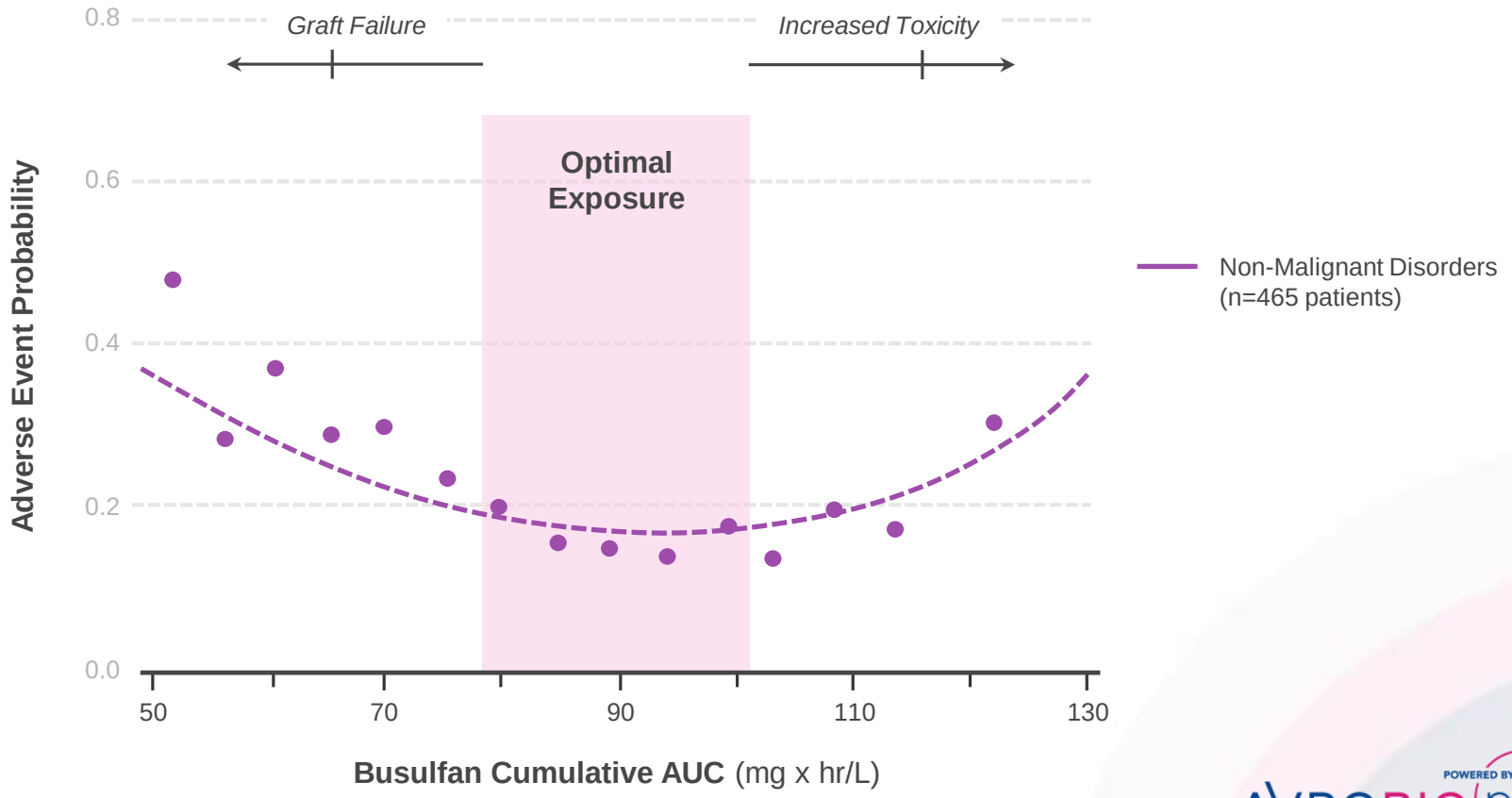
PRECISION CONDITIONING UPGRADE:

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



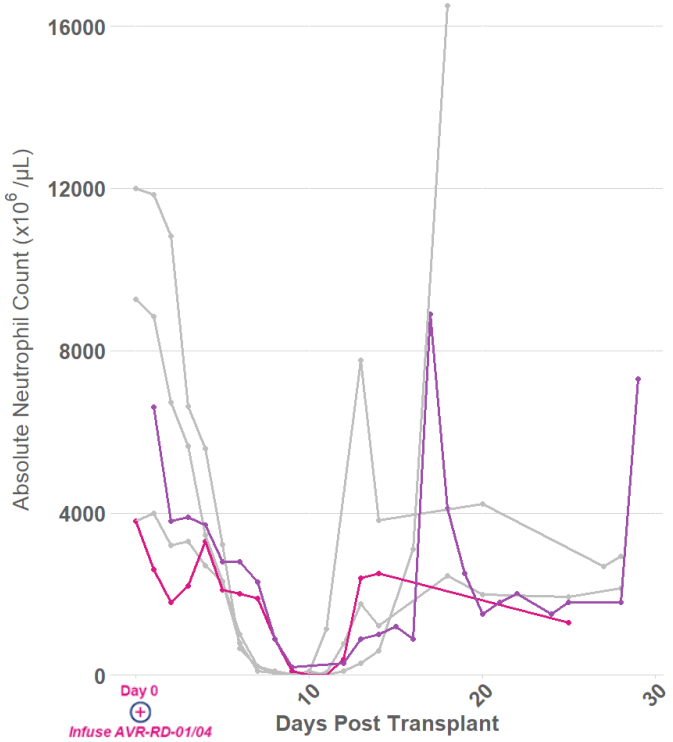
Bu: Busulfan; AUC: Area Under the Curve
Sources: Bartelink IH et al, Lancet Haematol, 2016

plato® UPGRADE 2

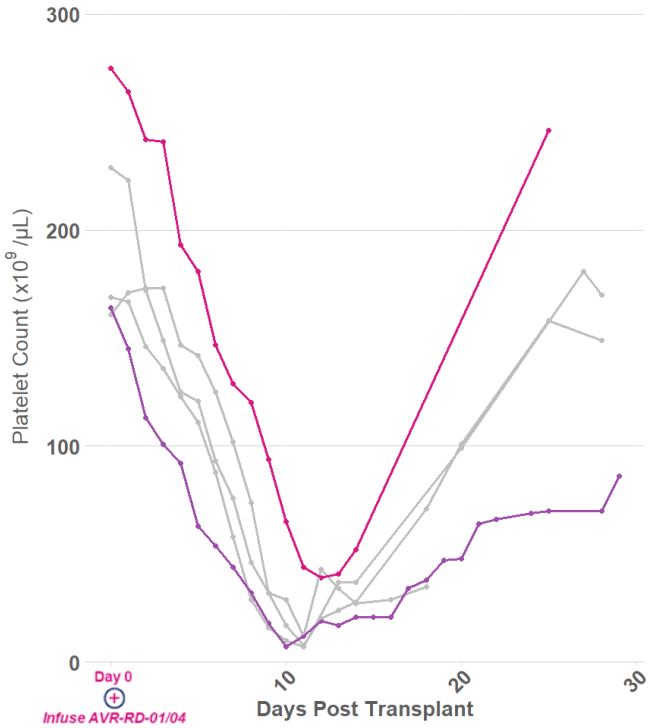
PRECISION CONDITIONING UPGRADE:

Rapid neutrophil and platelet recovery with minimal lymphocyte depletion using Busulfan TDM

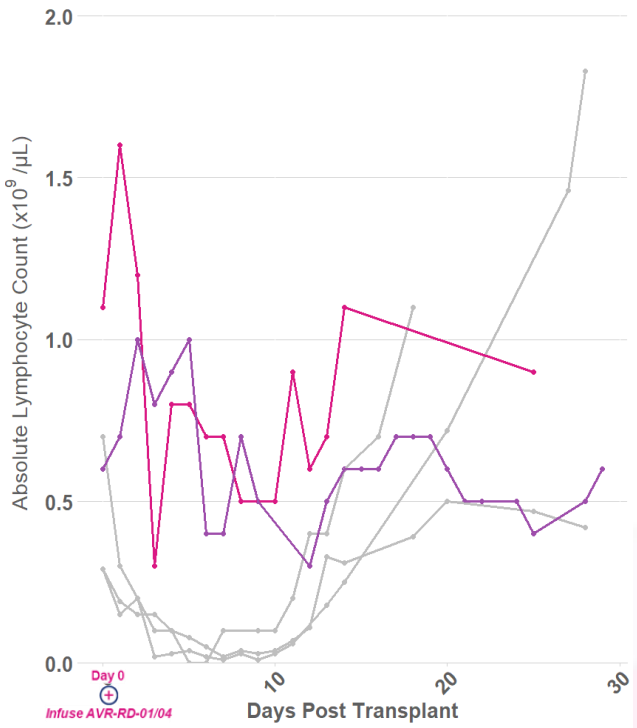
Absolute Neutrophil Count (ANC)



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 x 10^9 per liter (AABB); Platelets <10 X 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

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plato® UPGRADE 3

AUTOMATION UPGRADE:

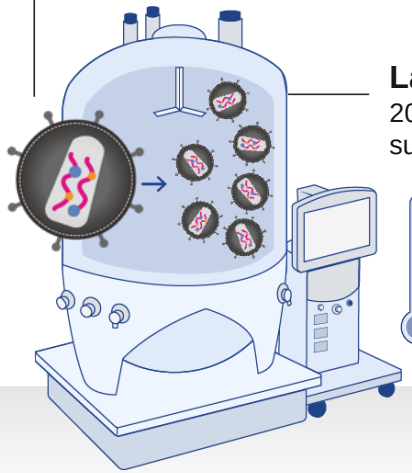
Designed to deliver large-scale manufacturing

Differentiated, cost-effective approach

1 Vector production → **2 Drug product production** → **3 Scalable, global production suites**

HIGH VOLUME / TITRE

Vector with disease-specific transgene

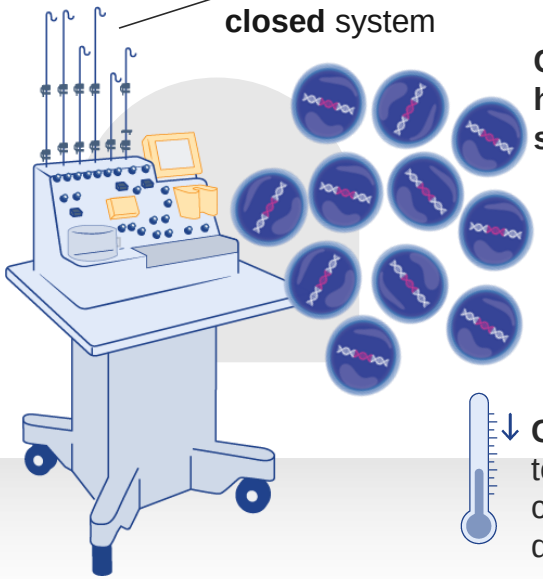


Large bioreactor
200 liter serum-free suspension culture

Frozen in aliquots to streamline supply chain

INCREASE CONSISTENCY

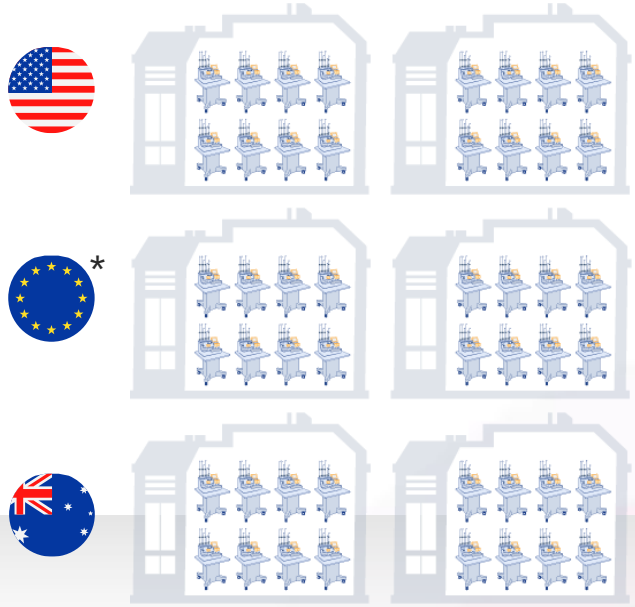
Automated, closed system



CD 34+ hematopoietic stem cells

Cryopreserved to enable convenient dosing

COST-EFFECTIVE SCALE-OUT



Illustrative

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

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plato® UPGRADE 1, 2, 3

3 UPGRADES IN PLACE:

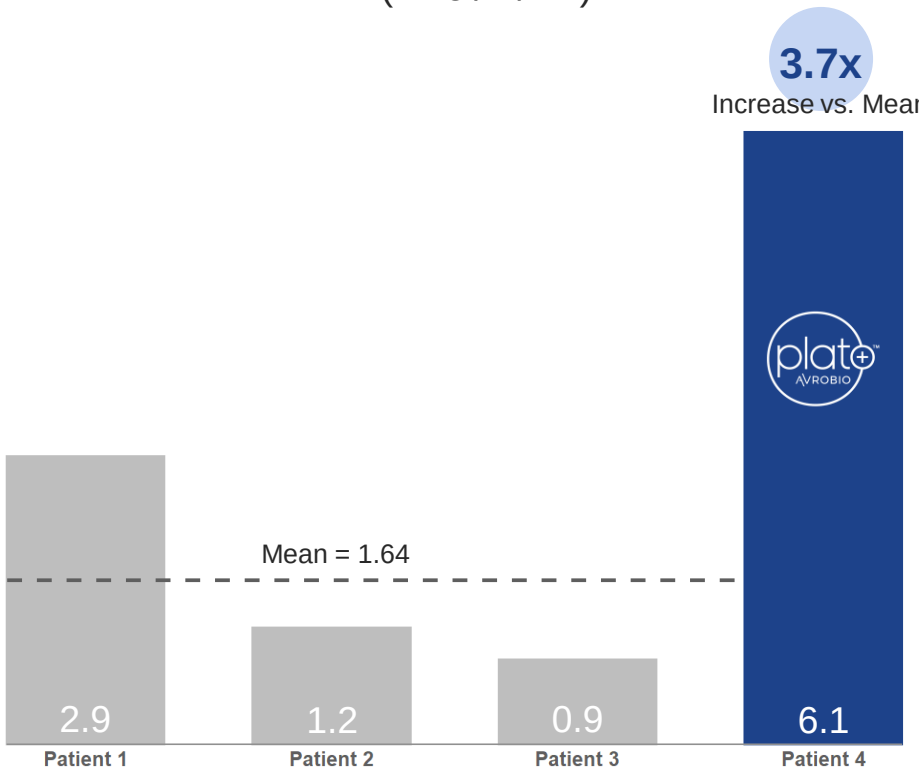
New data point

plato® metric compared to academic process

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

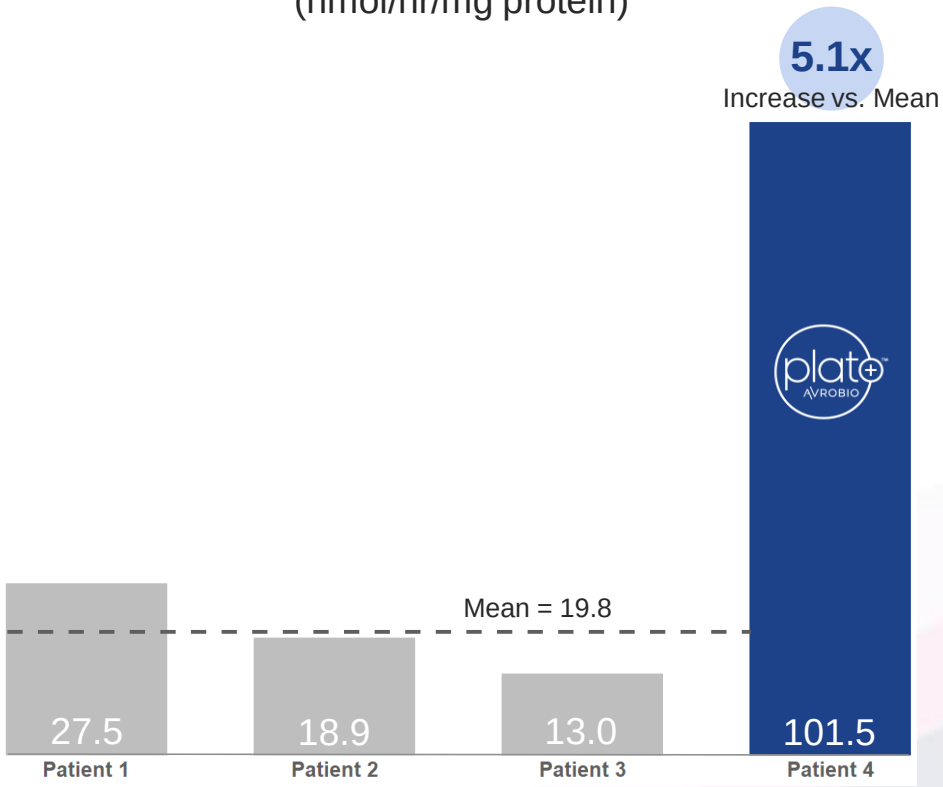
Plasma Enzyme Activity

(nmol/hr/mL)



Leukocyte Enzyme Activity

(nmol/hr/mg protein)



FAB-201: AVR-RD-01 Study

POWERED BY plato™

Milestones anticipated across the pipeline in 2020

Clinical activities and timelines subject in all respects to ongoing and evolving COVID-19 pandemic*

FABRY

- Continue recruitment in FAB-201 Phase 2 clinical trial
- Continue to report patient data across Phase 1 and Phase 2 clinical trials

GAUCHER

- Continue recruitment in GuardOne Phase 1/2 clinical trial
- Report initial patient data in H2 2020

CYSTINOSIS

- Continue recruitment in investigator-sponsored Phase 1/2 clinical trial
- Continue to report patient data

POMPE

- Complete preclinical IND-enabling activities

AVROBIO to hold first R&D Day in Q4 2020

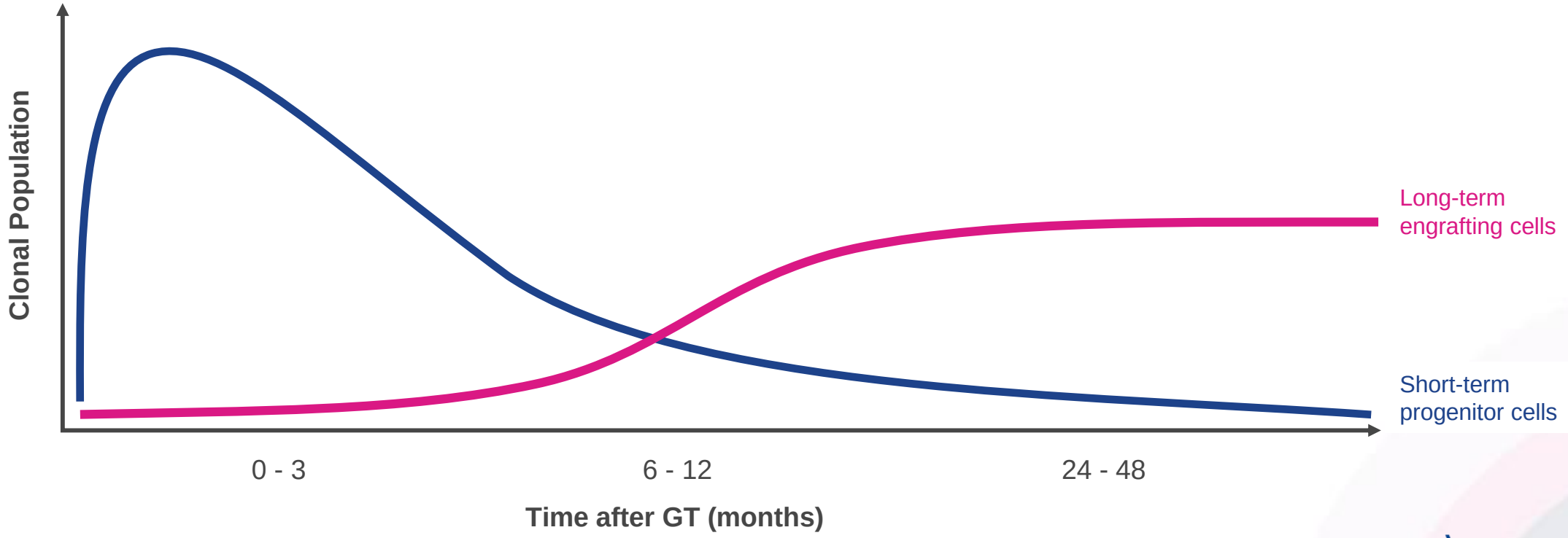
* For additional information, see the Company's Quarterly Report on Form 10-Q filed with the SEC on August 6, 2020.

Appendix

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: Biasco L et al, Cell Stem Cell, 2016

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

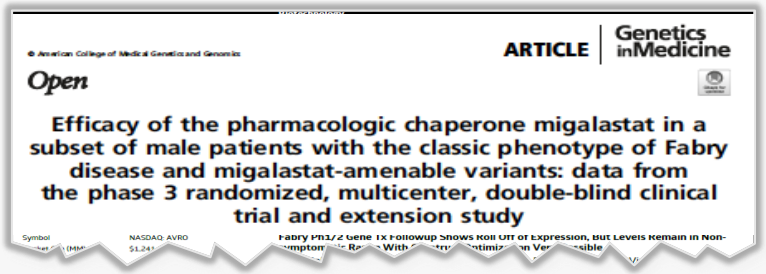
45 Amenable patients* (16 males / 29 females)

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)


American College of Medical Genetics and Genomics

ARTICLE | Genetics inMedicine

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

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

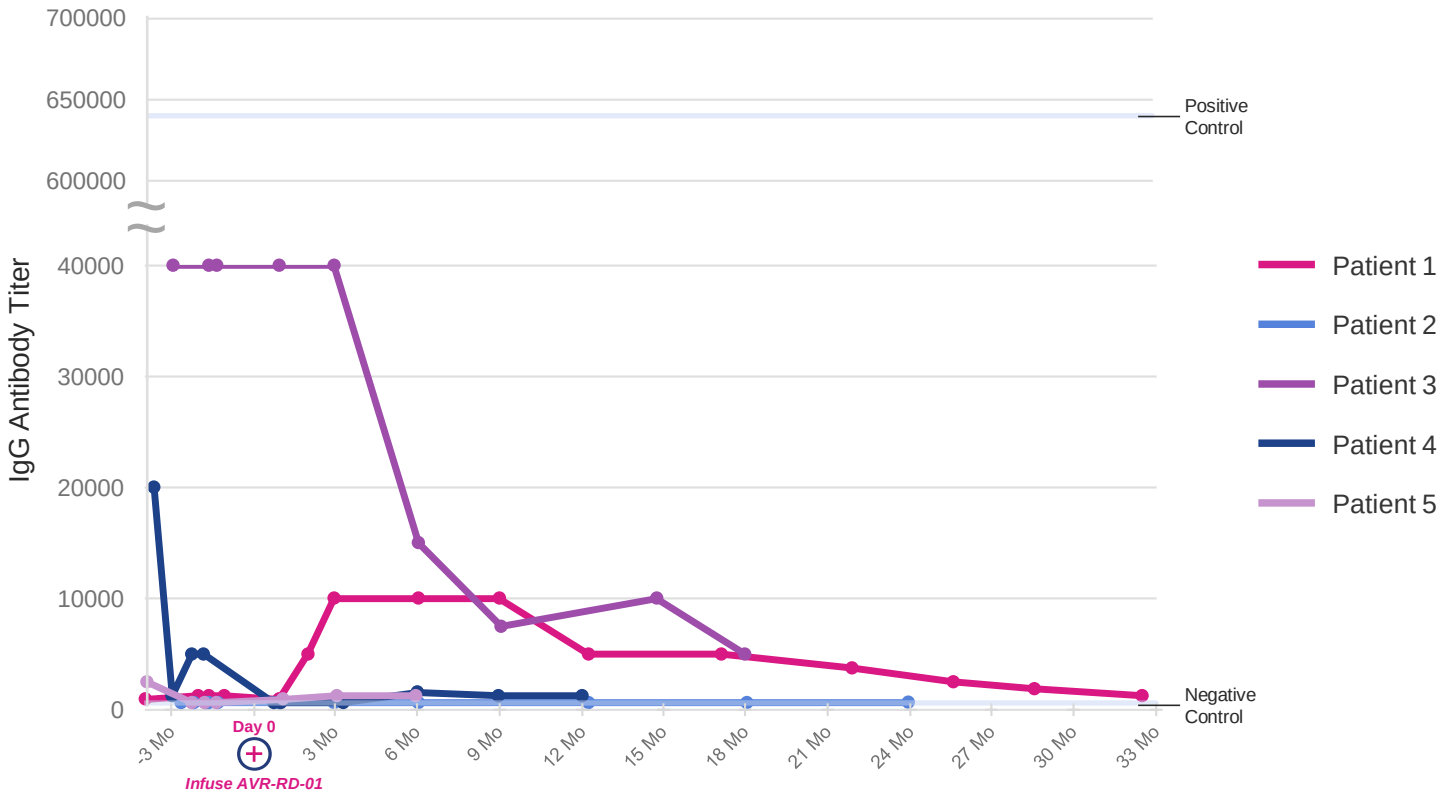
46% average reduction
(average of patients with 12 month data)

- *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*

Reduction of pre-existing anti-ERT drug IgG antibodies following AVR-RD-01

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

Fabry Disease Phase 1 IgG Antibody Titer



Similar Results Observed in Other Studies

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

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

- Ex vivo LV-CD34+ gene therapy with conditioning
- N = 6
- Evaluable patients (5/6) demonstrated sustained, supraphysiologic blood IDUA activity
- 4/5 prior ERT (rhIDUA) exposure (5-28 months)
- 4/5 pre-existing ERT-induced IgG antibodies
- 6/6 anti-rhIDUA IgGs undetectable 2 months post gene therapy

Source: *Gentner B et al., Blood, 2019*

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

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