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THE GREAT POTENTIAL TO CURE

Fabry Data Update: October 2018

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Our Mission

Curing rare disease in a single dose.

Just as enzyme replacement therapies (ERTs) revolutionized the past, gene therapy has the potential to revolutionize the future.

Key Takeaways From Data Announcement

Overarching Points

- All patients continue to demonstrate α-galactosidase-A (AGA) enzyme activity above the diagnostic range for classic Fabry disease
- Patient #1 in the Phase 1 Study has had ERT discontinued; no reported severe adverse events (SAE) related to AVR-RD-01

Fabry Phase 1 Study (ERT)

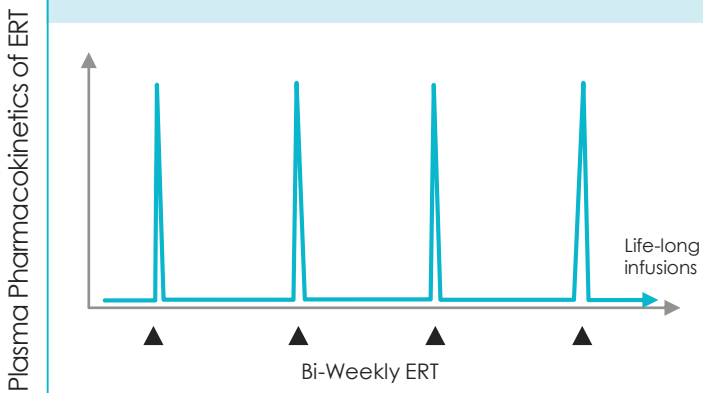
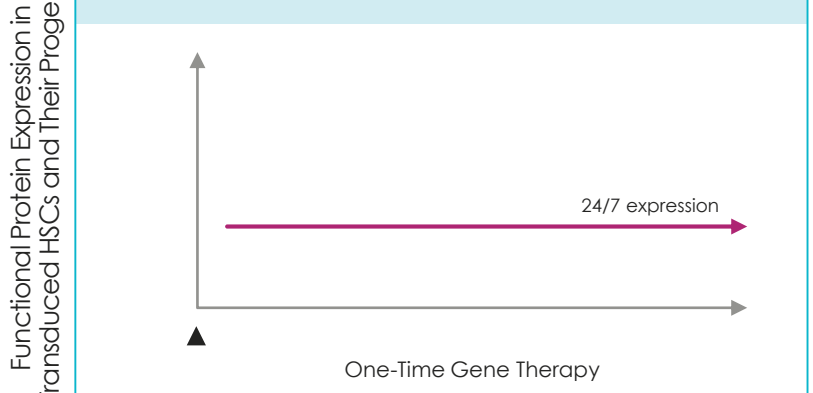
- Patient #1 enzyme activity is 2.6 nmol/hr/ml at 18 months, vector copy number (VCN) is 0.1, and ERT discontinued as of July 13, 2018
- Patient #2 enzyme activity is 3.7 nmol/hr/ml at 6 months and VCN is 0.4
- Patient #3 was dosed in July 2018

Fabry Phase 2 Trial (ERT naïve - FAB-201*)

- First patient in ERT-naïve FAB-201 demonstrates plasma AGA enzyme activity above the diagnostic range for classic Fabry disease (enzyme activity is 2.7 nmol/hr/ml and VCN is 0.5 at 3 months)
- Safety profile of AVR-RD-01 remains within expectations and data safety monitoring committee (DSMC) has cleared path to consent patient #2
- Global study site expansion and platform optimization on track for 2019

*official name is AVRO-RD-01-201, the phase 2 clinical trial of AVR-RD-01

Life-Long Treatments vs. Single Dose Potential Cure

	Disease Progression ***Continues***	*Disease Progression* ***Can Halt***
	Enzyme Replacement Therapy (ERT) Temporary bolus of enzyme, not curative	**AVROBIO Gene Therapy** 24/7 expression of protein, curative potential
		
Enzyme or protein level	Transient, intermittent elevation	Long-term, continuous elevation
Treatment burden	Bi-weekly IV infusions	Single IV infusion

AVR-RD-01

Fabry Disease and Treatment Overview

Fabry is a Serious Rare Genetic Disease

Disease

- Mutations in α-galactosidase A (AGA) gene result in deficient enzyme activity
- Leads to accumulation of globotriaosylceramide (Gb3)

Impact

- Premature mortality (life expectancy decreased by 20 years in classic males)
- Cardiac disease, progressive renal failure, stroke, GI distress, acroparesthesias, anhidrosis, debilitating pain, fatigue

Standard of Care – ERT

- Not curative, relentless progression of disease continues
- Burdensome and expensive

Population Estimates

- 1:40,000 male live births (classic males) and 1:118,000 females

Sources: Meikle PJ et al, JAMA, 1999; Desnick R, J Inherit Metab Dis, 2001

AVR-RD-01

Phase 1 Investigator-Sponsored Study Data Update

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Ongoing Investigator-Sponsored Phase 1 Fabry Study

Fabry Patients

Day -30	Day -1	Day 0	Day 28	Day 30
Stop ERT Mobilize stem cells	Mild conditioning	Infuse AVR-RD-01	Post-treatment assessment	Re-start ERT

Clinical Pilot Study of Autologous Stem Cell Transplantation of CD34+ Cells Engineered to Express AGA in Patients with Fabry Disease

Inclusion Criteria	Objectives	Patients	Assess
• Safety • Preliminary efficacy	• Safety • Preliminary efficacy	• Up to 6 patients • 18-50 year old males • Receiving ERT	• Plasma and leukocyte enzyme activity • Presence of vector in peripheral blood and bone marrow cells • Safety

Fabry Phase 1 Study: Patient Characteristics

Patient #1

- 48 year old male; has been receiving ERT since 2005
- Medical history: Significant for urinary urgency, abdominal pain, proteinuria, angiokeratomas and left ventricular hypertrophy
- ***Patient had ERT discontinued in July 2018***

Patient #2

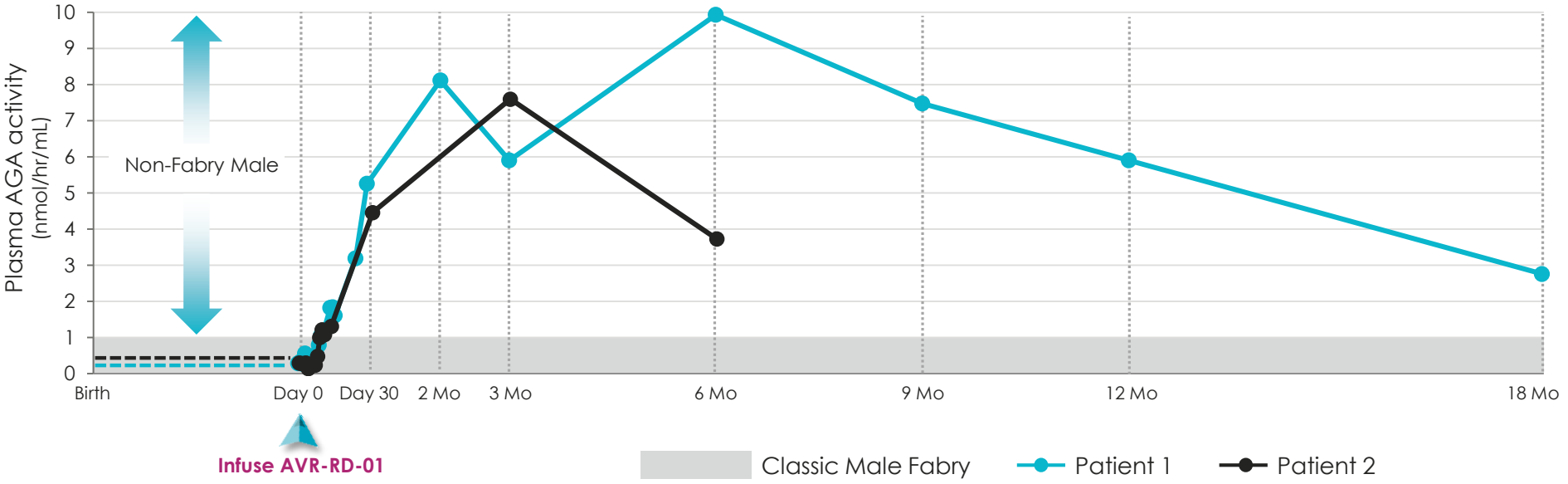
- 39 year old male; has been receiving ERT since 2011
- Medical history: Significant for peripheral sensory neuropathy, cold and heat intolerance, hypohidrosis, angiokeratomas, gastrointestinal issues, increased albumin to creatinine ratio, limb edema, corneal whorls, chronic kidney disease and proteinuria and cysts

Patient #3

- 39 year old male; has been receiving ERT since 2014
- Medical history: Significant for acroparesthesias, tinnitus, sinus bradycardia, type 1 Chiari malformation, left ventricular hypertrophy, dizziness, corneal verticillata, headache, atrial fibrillation, and palpitations

Fabry Phase 1 Study: Significant Enzyme Activity Elevation After Single Dose

Level of AGA Enzyme Activity Rose from Nearly Undetectable Levels to Levels Above the Range for Males with Classic Fabry Disease



Fabry Phase 1 Study: Peripheral Blood Average VCN

VCN Sample	Patient 1	Patient 2	Patient 3
Drug Product	0.7	1.4	0.8
1 Month post-treatment	0.4	0.8	0.2
3 Months post-treatment	0.6	1.1	
6 Months post-treatment	0.4	0.4	
9 Months post-treatment	0.3		
12 Months post-treatment	0.2		
18 Months post-treatment	0.1		

Patient #1 Bone marrow aspirate data at 14 months continues to support engraftment with a colony forming unit assay result of 13%

AVR-RD-01

FAB-201 (AVR-RD-01-201), Phase 2 Company-Sponsored Trial Data Update

FAB-201: First Patient Dosed June 7

Phase 2 Open-Label, Multinational Study of the Efficacy and Safety of *Ex Vivo* Lentiviral-Based Vector Gene Therapy AVR-RD-01 for Treatment-Naïve Subjects with Classic Fabry Disease

Objectives	Patients	Assess
• Efficacy (biomarkers and functional endpoints) • Safety	• 8-12 patients • Adult males (age ≥ 16 years) • Treatment-naïve	• Primary efficacy endpoint: reduction of substrate in kidney biopsy • Substrate reduction (Gb_3 and/or lyso-Gb3) in urine, plasma, skin • Enzyme (AGA) activity • Kidney function • Cardiac size • GI symptoms • Pain and quality of life • Vector Copy Number (VCN) and chimerism • Safety

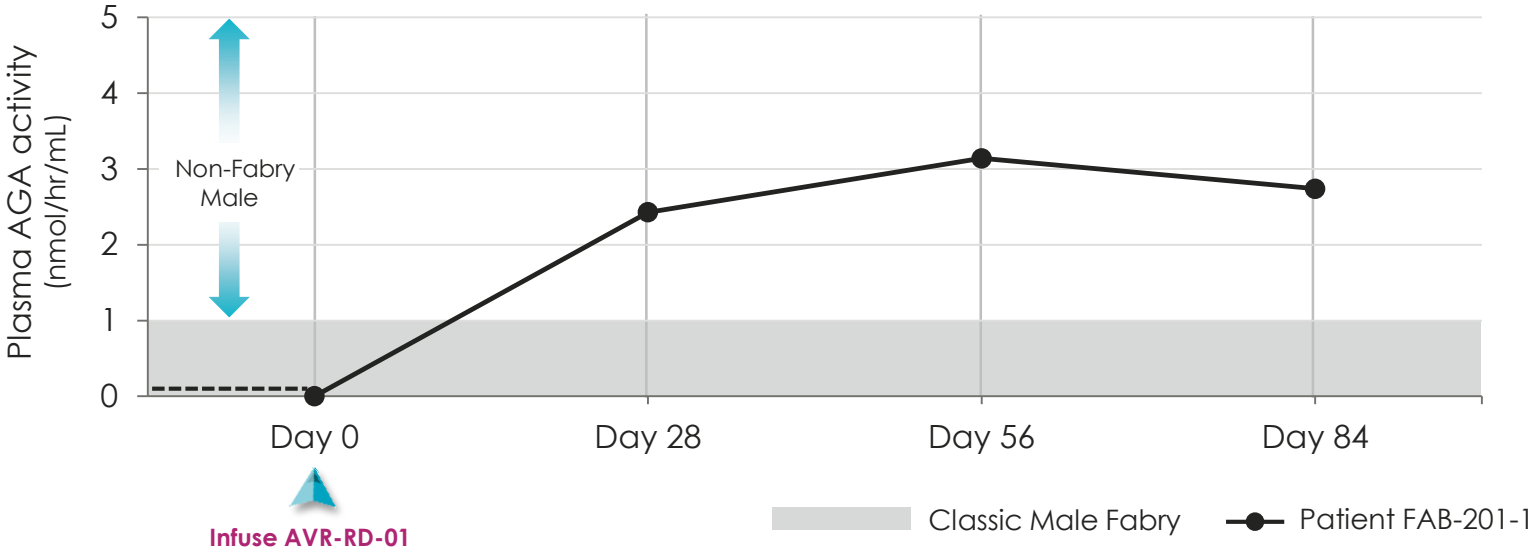
FAB-201: Patient Characteristics

Patient FAB-201-1

- 21 year old male
- Has not received any prior treatment with ERT
- Medical history: Significant for chronic acral pain, knee pain, intermittent diarrhea, traumatic eye injury, pansinusitis, umbilical keratoma, chronic obstructive pulmonary disease, decreased cold sensation, and epilepsy

FAB-201: Significant Enzyme Activity Elevation After Single Dose

Level of AGA Enzyme Activity Rose from Nearly Undetectable Levels to Levels Above the Range for Males with Classic Fabry Disease



FAB-201: FAB-201-1 Peripheral Blood Average VCN

VCN Sample	Patient FAB-201-1
Drug Product	0.7
1 month post-treatment	0.2
2 months post-treatment	0.2
3 months post-treatment	0.5

AVR-RD-01

Safety and Tolerability

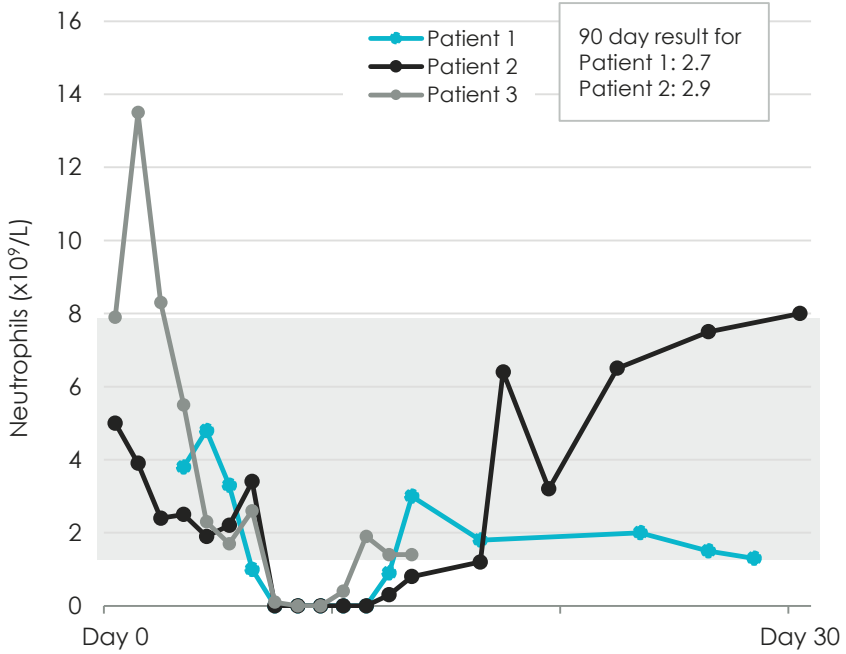
Safety and Tolerability of AVR-RD-01

- First three enrolled subjects in Phase 1 investigator-sponsored study*
  - AVR-RD-01 was generally well tolerated
  - No serious adverse events related to AVR-RD-01
- FAB-201-1 (first patient in FAB-201)**
  - AVR-RD-01 was generally well tolerated
  - Two serious adverse events reported, one pre-treatment and one post-treatment (dehydration, nausea and vomiting), neither was considered related to AVR-RD-01

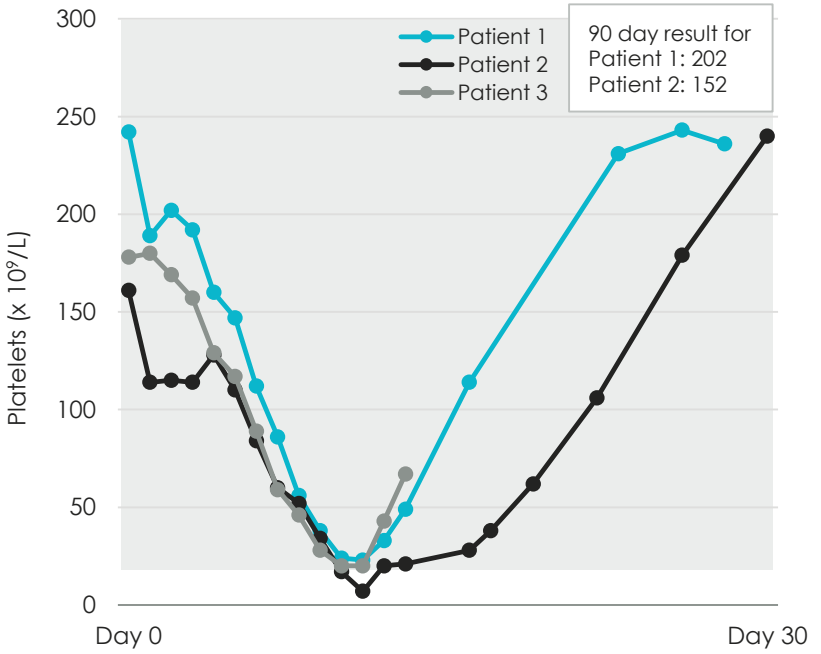
*data cutoff date: August 24, 2018
**data cutoff date: August 28, 2018

Conditioning to Develop First-Line Therapies: Fabry Phase 1

Neutrophil Count Recovery



Platelet Count Recovery

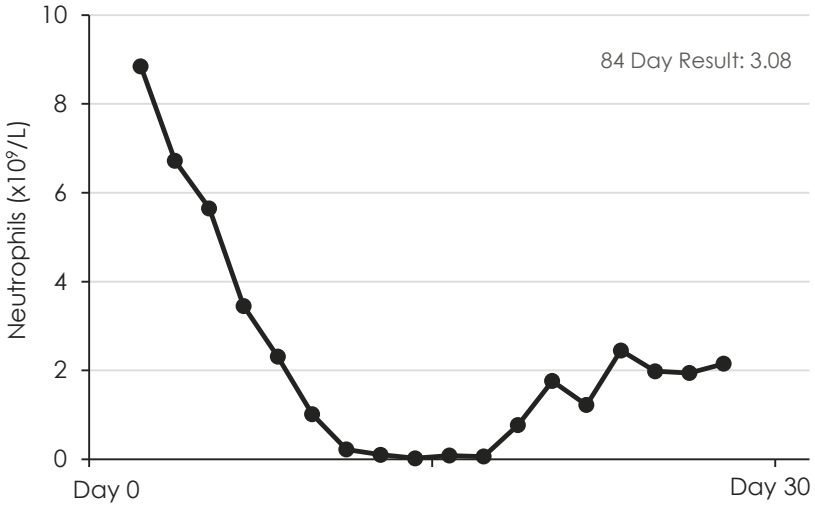


Melphalan 100mg/m^2 IV on Day -1

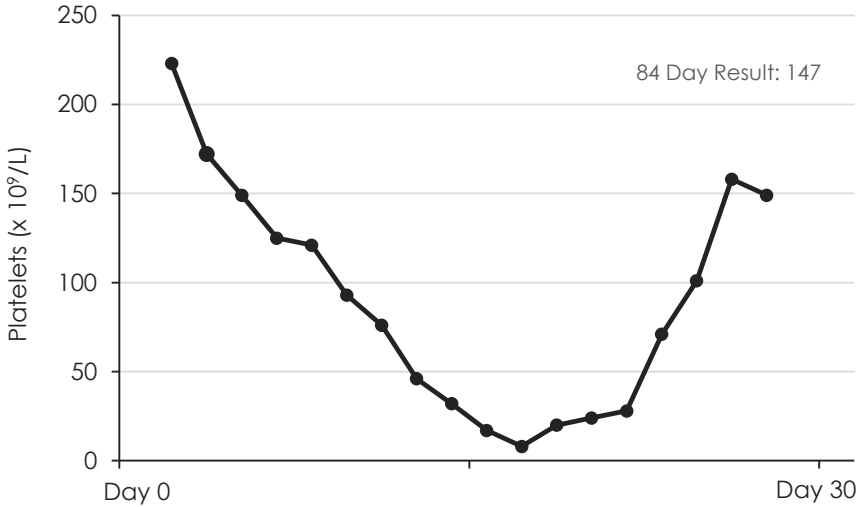
Note: Neutrophil count lower range defined as when patients no longer require GCSF support per OZM-074 protocol
Note: Platelet count lower range defined as when platelet transfusion support would be considered clinically given increased risk of spontaneous bleeding

FAB-201-1: Conditioning to Develop First-Line Therapies

Neutrophil Count Recovery



Platelet Count Recovery



Patient FAB-201-1

Melphalan 100mg/m^2 IV on Day -1

AVR-RD-01

Next Steps and Summary of Key Findings

AVR-RD-01 Next Steps

Next steps

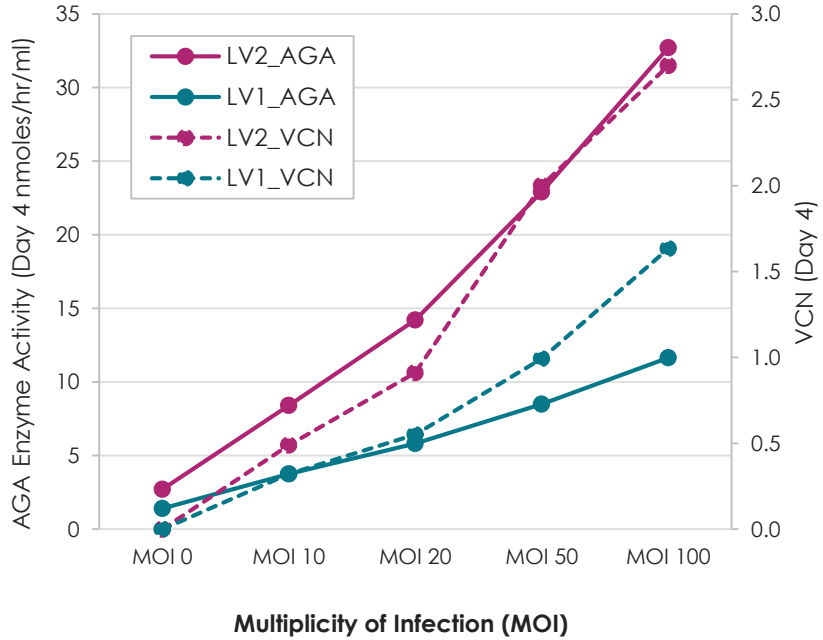
- Ongoing recruitment of both the Phase 1 and Phase 2 Fabry clinical trials
- Expansion of FAB-201 clinical sites to USA and Japan
- Continued CMC progress toward platform optimization

Global Sites and Platform Optimization in FAB-201

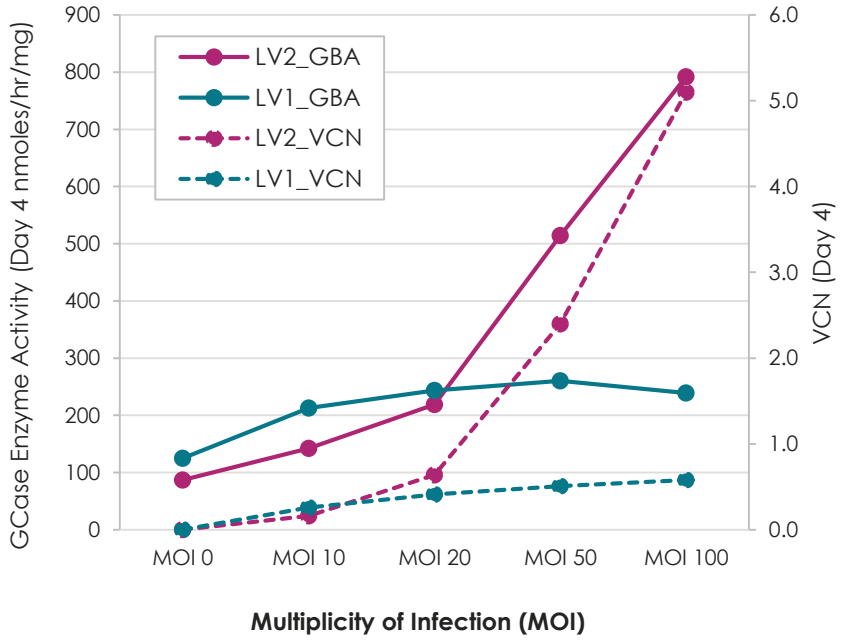
2018	2019	2020
Canada Australia	Canada Australia USA	Canada Australia USA Japan
Ongoing platform optimization		

Ongoing Vector Optimization Enhances Efficiency

LV2 v. LV1 Fabry Performance*



LV2 v. LV1 Gaucher Performance*



* CMC data

AVR-RD-01: Summary of Key Findings

Fabry Phase 1 Study (ERT)

- All patients continue to demonstrate AGA enzyme activity above the diagnostic range for classic Fabry disease
- Patient #1 has had ERT discontinued with no reported SAE's related to AVR-RD-01
- Patient #1 enzyme activity and VCN will continue to be monitored for long-term durability

FAB-201 (ERT-naïve patients)

- FAB-201-1 demonstrates AGA enzyme activity above diagnostic range at 3 months
- Safety profile of AVR-RD-01 remains within expectations and DSMC has cleared path to consent next patient