



AVROBIO Announces Updated Clinical Data for AVR-RD-01 Gene Therapy in Fabry Disease

First two patients in Phase 1 study continue to demonstrate AGA enzyme activity above the diagnostic range for classic Fabry disease 18 months and six months after receiving AVR-RD-01, respectively; Patient 1 is no longer receiving enzyme replacement therapy

Enrollment continues in Phase 2 clinical trial and first patient's 3-month results demonstrate AGA enzyme activity from AVR-RD-01 gene therapy in ERT-naïve patient

Company to host a conference call to discuss these additional data today, October 1, 2018 at 8:30 a.m. ET

CAMBRIDGE, Mass.— October 1, 2018 – [AVROBIO, Inc.](#) (Nasdaq: AVRO) (the “Company”), a Phase 2 clinical-stage gene therapy company developing gene therapies to potentially cure rare diseases with a single dose, today announced clinical data and patient updates from the investigator-sponsored Phase 1 study and the AVROBIO-sponsored Phase 2 clinical trial of AVR-RD-01. AVR-RD-01 is an *ex vivo* lentiviral gene therapy being investigated in [Fabry disease](#). Designed to be a one-time therapy, it works by inserting the GLA gene that encodes functional α -galactosidase A (AGA, the enzyme that is deficient in Fabry disease) to enable continuous AGA production and distribution to tissues and organs.

The investigator-sponsored Phase 1 study is designed to assess the safety of AVR-RD-01 in up to six patients with Fabry disease who have been treated with standard of care enzyme replacement therapy (ERT) for at least six months prior to receiving AVR-RD-01. The Phase 1 study is conducted by the FACTs team (Fabry disease Clinical research and Therapeutics) in Canada and led by their principal investigator, Jeffrey A. Medin, Ph.D. The AVROBIO-sponsored Phase 2 trial of AVR-RD-01 (the FAB-201 Study¹) is an open-label, single-arm clinical trial evaluating the efficacy and safety of AVR-RD-01 in eight to twelve treatment-naïve patients.

“We are encouraged by the AGA enzyme activity we are seeing after treatment with AVR RD-01 in the first two patients with Fabry disease in the Phase 1 study. Both of these patients have AGA activity that remains above the diagnostic range for males with classic Fabry disease, and all patients will continue to be followed for assessment of long-term durable response. We are especially pleased that patient 1 was taken off ERT in mid-July and remains off,” said Geoff MacKay, President and CEO of AVROBIO. “We recently achieved an important milestone in dosing

the first patient in our ERT-naïve Phase 2 FAB-201 trial. This patient is now demonstrating AGA activity above the diagnostic range for males with classic Fabry disease three months after receiving our gene therapy treatment. In parallel, we continue our move towards implementation of a set of process optimization initiatives, including heightened vector efficiency, our fully closed, automated manufacturing system and conditioning.”

Key results from the three patients who have been dosed with AVR-RD-01 in the ongoing Phase 1 clinical study, include:

- **Patient 1:** At 18 months after AVR-RD-01 treatment, AGA enzyme activity was 2.6 nmol/hr/ml, which is above the diagnostic range for males with classic Fabry disease (defined as less than 1 nmol/hr/ml), and average vector copy number (VCN) in peripheral blood was 0.1. VCN refers to the average number of copies of the lentiviral-vector inserted gene that are integrated into the genome of a cell. Bone marrow aspirate data at 14 months continues to support engraftment of cells that are producing progeny with the vector inserted.

After the 18-month follow-up visit for patient 1, the FACTs team investigators received approval, and the patient consented, to discontinue the regular bi-weekly treatment with ERT. Patient 1 will continue to be monitored to evaluate his AGA enzyme activity following discontinuation of ERT.

- **Patient 2:** At six months after AVR-RD-01 treatment, AGA enzyme activity (3.7 nmol/hr/ml) also remained above the diagnostic range for males with classic Fabry disease and the VCN was 0.4.
- **Patient 3:** In July 2018, the third patient with Fabry disease was dosed with AVR-RD-01 in the Phase 1 study.
- As a Phase 1 study, the primary endpoint of this study is safety. Preliminary safety data from these three subjects indicate AVR-RD-01 was generally well tolerated and no serious adverse events (SAEs) related to AVR-RD-01 have been reported (as of the safety data cut-off date of August 24, 2018).
- Continued patient enrollment is planned and the protocol has been amended to allow the FACTs team, at their discretion, to discontinue ERT six months after treatment with AVR-RD-01.

“We particularly highlight the 18-month data from patient 1 who maintained AGA enzyme activity above the diagnostic range for classic Fabry disease and we received approval to discontinue ERT and observe the impact of gene therapy alone,” said Dr. Aneal Khan of the FACTs team. “We

continue to advance our efforts for a one-time gene therapy that transforms the lives of patients with this chronic, progressive disease.”

In the Phase 2, FAB-201 Study, data is reported from the first patient who has been dosed with AVR-RD-01:

- **Patient FAB-201-1:** Data for the first patient, FAB-201-1, in the Phase 2 trial demonstrated that after three months of treatment with AVR-RD-01, AGA plasma enzyme activity was 2.74 nmol/hr/ml and VCN was 0.5.

Preliminary safety data from patient FAB-201-1 indicate that AVR-RD-01 was generally well tolerated; no SAEs related to AVR-RD-01 have been reported (as of the safety data cut-off date of August 28, 2018.) Enrollment in the FAB-201 Study is ongoing.

Further details of the Phase 2, FAB-201 Study of AVR-RD-01 in Fabry disease are available on clinicaltrials.gov.²

These interim results from the investigator-sponsored Phase 1 study and the AVROBIO-sponsored Phase 2 trial are also scheduled to be presented at the 1st Canadian Symposium on Lysosomal Diseases (CLSD) in Sherbrooke, Quebec, on October 5-6, 2018, and at the 26th Annual Congress of the European Society of Cell & Gene Therapy (ESCGT), in Lausanne, Switzerland, on October 16-19, 2018.

Conference Call and Webcast Information

AVROBIO will host a conference call and webcast on Monday, October 1, 2018 at 8:30 a.m. ET to review the updated clinical data. The event will be webcast live and can be accessed under “Calendar of Events” 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 2669262.

About AVR-RD-01

[AVR-RD-01](#) is an *ex vivo* lentiviral gene therapy being investigated as a single-dose therapy with the potential to provide durable and life-long potential therapeutic benefit for patients with [Fabry disease](#). AVR-RD-01 is designed to employ a state-of-the-art [lentiviral vector platform](#) that is an efficient and proven gene transfer system for the permanent integration of a functional copy of the gene 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 GLA gene that encodes α -galactosidase A (AGA) – the enzyme that is deficient in Fabry disease – to create AVR-RD-01 gene therapy. AVR-RD-01 is then infused back into the patient with the goal of restoring normal GLA gene expression such that functional AGA enzyme is sufficiently produced by the patient’s own body.

About AVROBIO, Inc.

[AVROBIO, Inc.](#), is a Phase 2 clinical-stage gene therapy company developing gene therapies to potentially cure rare diseases with a single dose. AVROBIO's [lentiviral-based gene therapies](#) employ hematopoietic stem cells that are collected from the patient and then modified with a lentiviral vector to insert a functional copy of the gene that is defective in the target disease. AVROBIO is focused on the development of its 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](#). AVROBIO is headquartered in Cambridge, MA and has offices in Toronto, ON. For additional information, visit www.avrobio.com.

Forward-looking Statements

Various express or implied statements in this release concerning AVROBIO's future expectations, plans and prospects, including without limitation, statements regarding the development and the continued progress of AVROBIO's programs, and the therapeutic potential of its product candidates, including AVR-RD-01, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Any forward-looking statements in this press release are based on management's current 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, including AVR-RD-01, will not be successfully developed or commercialized, the risk of cessation or delay of any of AVROBIO's ongoing or planned clinical trials, and the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies or clinical trials will not be replicated or will not continue in ongoing or future studies or trials involving AVROBIO's 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, as well as other risks detailed 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.

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

² FAB-201 Study on clinicaltrials.gov:

<https://clinicaltrials.gov/ct2/results?cond=&term=AVROBIO&cntry=&state=&city=&dist=>

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