Press Release Details

AVROBIO Announces New Patients Dosed in Gaucher Disease and Cystinosis Clinical Trials

First patient dosed in AVROBIO's global Phase 1/2 clinical trial of AVR-RD-02 for Gaucher disease type 1

Second patient dosed in investigator-sponsored Phase 1/2 clinical trial of AVR-RD-04 for cystinosis

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 6, 2020-- AVROBIO, Inc. (Nasdaq: AVRO), a leading clinical-stage gene therapy company with a mission to free people from a lifetime of genetic disease, today announced that the first patient has been dosed in the company's GuardOne clinical trial, a Phase 1/2 investigational study evaluating AVR-RD-02 for Gaucher disease type 1. The company also announced that the second patient has been dosed in the ongoing investigator-sponsored Phase 1/2 clinical trial of AVR-RD-04 for cystinosis.

"The first patient dosed is an important milestone for the Gaucher disease community and our AVR-RD-02 program. Gaucher disease type 1 leads to an array of serious symptoms and the current standard of care does not halt disease progression," said Geoff MacKay, AVROBIO's president and CEO. "With a single dose of our investigational lentiviral gene therapy, we aim to prevent the buildup of a fatty substrate in specialist immune cells called macrophages, as well as debilitating symptoms throughout the body, including the brain."

The company's Phase 1/2 trial of AVR-RD-02 for Gaucher disease type 1 is currently recruiting patients in Australia and Canada, with new clinical sites expected to open in the U.S. and Israel by year-end.

Gaucher disease is a rare, inherited lysosomal storage disorder characterized by the toxic accumulation of glucosylceramide (GlcCer) and glucosylsphingosine (GlcSph) in macrophages. Macrophages bloated with these fatty substances are called Gaucher cells which amass primarily in

the spleen, liver and bone marrow. This results in a variety of potential symptoms, including grossly enlarged liver and spleen, bone issues, fatigue, low hemoglobin levels and platelet counts and an adjusted lifetime relative risk of developing Parkinson's disease that may be more than 20 times greater than the general population. Even on enzyme replacement therapy (ERT) – the current standard of care – people with Gaucher disease type 1 have a shortened life expectancy and may experience debilitating symptoms that significantly reduce their quality of life. An estimated 1 in 44,000 people are diagnosed with Gaucher disease.

“While the current treatments for Gaucher disease -- enzyme replacement therapy and substrate reduction therapy -- have been life changing, many unmet needs remain that significantly impact the daily lives of patients and families living with Gaucher disease, including fatigue, severe bone pain, joint destruction, increased risk of developing Parkinson’s disease and other co-morbidities,” said Christine White, executive director, National Gaucher Foundation of Canada. “We welcome clinical trials of new therapeutics that have the potential to stop the progression of Gaucher disease and are excited to learn more about the potential use of this lentiviral gene therapy.”

The Phase 1/2 trial of AVR-RD-02 for Gaucher disease type 1 is designed to evaluate the safety and efficacy of the investigational gene therapy and is expected to enroll eight to 16 patients between the ages of 18 and 35. AVR-RD-02 starts with the patient’s own hematopoietic stem cells, which are genetically modified to express functional glucocerebrosidase (GCase), the enzyme that is deficient in Gaucher disease. The trial will include both patients who are treatment-naïve and who are on ERT. Every patient in this trial will be treated using the plato® gene therapy platform, AVROBIO’s foundation designed to scale gene therapy worldwide.

Second patient dosed in cystinosis clinical trial

The second patient has been dosed in the company’s AVR-RD-04 investigational gene therapy program for cystinosis. The ongoing Phase 1/2 clinical trial is sponsored by the company’s academic collaborators at the University of California, San Diego (UCSD)[1] and is led by Stephanie Cherqui, Ph.D., associate professor of pediatrics at UCSD.

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

The Phase 1/2 clinical trial is evaluating the safety and efficacy of AVR-RD-04 in patients at least 18 years of age who are currently being treated with cysteamine. The trial will enroll up to six patients. AVR-RD-04 starts with the patient’s own hematopoietic stem cells, which are genetically modified to produce functional cystinosin, the protein that is deficient in cystinosis.

Patient recruitment activities for Fabry Phase 2 trial ongoing

Patient recruitment activities for AVROBIO’s Phase 2 FAB-201 trial for Fabry disease continue for clinical trial sites in Australia, Canada and the U.S. While clinical trial sites are starting to reopen and patient identification activities are ongoing with a number of potential new patients identified, activities related to new patient screening, consent and enrollment in the FAB-201 clinical trial have been slowed because of the COVID-19 pandemic.

AVROBIO is conducting two clinical trials for its AVR-RD-01 investigational gene therapy for Fabry disease. Four patients have been dosed in the global Phase 2 trial (FAB-201), which is evaluating treatment-naïve patients, and five patients are participating in the fully enrolled Phase 1 investigator-led clinical trial, known as FACTs.

AVR-RD-01 starts with the patient's own hematopoietic stem cells, which are genetically modified to produce functional alpha-galactosidase A, the enzyme that is deficient in Fabry disease. People with the disease experience a toxic buildup of a complex cell lipid called globotriaosylceramide (Gb3 or GL3), which can damage tissues throughout the body and brain, and cause the progressive signs and symptoms of Fabry disease.

About AVROBIO's personalized gene therapy approach

Our investigational lentiviral gene therapies start with the patient's own hematopoietic stem cells. We use a lentiviral vector to transduce those cells in order to insert a therapeutic gene designed to enable the patient to produce a supply of the functional protein they lack. These cells are then infused back into the patient, where they are expected to engraft in the bone marrow and produce generations of daughter cells, each containing a copy or copies of the therapeutic gene. To optimize engraftment, we use a personalized conditioning regimen with precision dosing of busulfan to make space and enable durable engraftment in the patient's bone marrow and central nervous system (CNS). Busulfan is an extensively validated conditioning agent generally considered to be the gold standard for ex vivo lentiviral gene therapy and has been administered to hundreds of patients for this purpose. Our approach is designed to drive durable production of the functional protein throughout the patient's body, thereby potentially addressing symptoms from "head to toe," including those originating in the CNS.

About lentiviral gene therapy

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

About AVROBIO

Our vision is to bring personalized gene therapy to the world. We aim to halt or reverse disease throughout the body by driving durable expression of functional protein, even in hard-to-reach tissues and organs including the brain, muscle and bone. Our clinical-stage programs include Fabry disease, Gaucher disease and cystinosis and we also are advancing a preclinical program in Pompe disease. AVROBIO is powered by the plato® gene therapy platform, our foundation designed to scale gene therapy worldwide. We are headquartered in Cambridge, Mass., with an office in Toronto, Ontario. For additional information, visit avrobio.com, and follow us on Twitter and LinkedIn.

Forward-Looking Statement

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words and phrases such as “aims,” “anticipates,” “believes,” “could,” “designed to,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will,” and variations of these words and phrases or similar expressions that are intended to identify forward-looking statements. These forward-looking statements include, without limitation, statements regarding our business strategy for and the potential therapeutic benefits of our prospective product candidates, including the ability to stop disease progression, the design, commencement, enrollment and timing of ongoing or planned clinical trials, including new patient screening, consent and enrollment activities in our FAB-201 clinical trial, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, the expected benefits and results of our implementation of the plato platform in our clinical trials and gene therapy programs, and the expected safety profile of our investigational gene therapies. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Results in preclinical or early-stage clinical trials may not be indicative of results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

Any forward-looking statements in this press release are based on AVROBIO’s current expectations, estimates and projections about our industry as well as management’s current beliefs and expectations of future events only as of today and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of AVROBIO’s product candidates will not be successfully developed or commercialized, the risk of cessation or delay of any ongoing or planned preclinical or clinical trials of AVROBIO or our collaborators, the risk that AVROBIO may not successfully recruit or enroll a sufficient number of patients for our clinical trials, the risk that AVROBIO may not realize the intended benefits of our gene therapy platform, including the features of our plato platform, the risk that our product candidates or procedures in connection with the administration thereof will not have the safety or efficacy profile that we anticipate, the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical or clinical trials, will not be replicated or will not continue in ongoing or future studies or trials involving AVROBIO’s product candidates, the risk that we will be unable to obtain and maintain regulatory approval for our product candidates, the risk that the size and growth potential of the market for our product candidates will not materialize as expected, risks associated with our dependence on third-party suppliers and manufacturers, risks regarding the accuracy of our estimates of expenses and future revenue, risks relating to our capital requirements and needs for additional financing, risks relating to clinical trial and business interruptions resulting from the COVID-19 outbreak or similar public health crises, including that such interruptions may materially delay our development timeline and/or increase our development costs or that patient enrollment and/or data collection efforts may be impaired or otherwise impacted by such crises, and risks relating to our ability to obtain and maintain intellectual property protection for our product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause AVROBIO’s actual results to differ materially and adversely from those contained in the forward-looking statements, see the section entitled “Risk Factors” in AVROBIO’s most recent Quarterly Report, as well as discussions of potential risks, uncertainties and other important factors in AVROBIO’s subsequent filings with the Securities and Exchange Commission. AVROBIO explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

[1] Collaborator-sponsored Phase 1/2 clinical trial of AVR-RD-04 is funded in part by grants to UCSD from the California Institute for Regenerative Medicine (CIRM), Cystinosis Research Foundation (CRF) and National Institutes of Health (NIH).

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