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): November 17, 2020

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 November 17, 2020, AVROBIO, Inc. (the "Company") issued a press release titled "AVROBIO Announces New Positive Clinical Data and Preclinical Data, as Well as Expanded Leading Lysosomal Disorder Gene Therapy Pipeline." 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Press release issued by AVROBIO, Inc., dated November 17, 2020.
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBRL.

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: November 17, 2020

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

Exhibit 99.1

AVROBIO Announces New Positive Clinical Data and Preclinical Data, as Well as Expanded Leading Lysosomal Disorder Gene Therapy Pipeline

Three months post-gene therapy, first patient in Gaucher trial shows reductions in the toxic metabolite plasma lyso-Gb1 and plasma chitotriosidase as compared to baseline when the patient was on ERT

Ongoing Fabry disease trials continue to demonstrate sustained durability, with first patient out 3.5 years

One year post-gene therapy, first patient in cystinosis trial remains off cysteamine, with positive data across multiple measures, including substantial reduction in cystine crystals in cornea

Clinical trial recruitment gaining momentum with five new patients expected to be dosed, enrolled or consented in 4Q 2020

Gaucher disease type 3 program added to pipeline; recently added Hunter syndrome program planned to enter clinic next year

Virtual R&D Day to be webcast today starting at 9 a.m. ET

CAMBRIDGE, Mass., Nov. 17, 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 positive new data across its clinical programs in Gaucher disease type 1, Fabry disease and cystinosis, further reinforcing the potential of ex vivo lentiviral gene therapy for lysosomal disorders. Additionally, AVROBIO is further expanding its lysosomal disorder pipeline with a new program in Gaucher disease type 3, which joins the recently announced program in Hunter syndrome in a synergistic portfolio of six programs designed to prevent, halt or reverse genetic disease.

“We’re delighted to report substantial new data across our three clinical programs. Three months post-gene therapy infusion, the first Gaucher disease patient’s levels of the toxic metabolite plasma lyso-Gb1, as well as plasma chitotriosidase, were lower than the baseline levels when the patient was still on enzyme replacement therapy (ERT). With our Fabry disease data continuing to reflect sustained and durable results, with our first patient now out 3.5 years from dosing, we are planning our strategy to seek accelerated approvals in one or more major markets,” said Geoff MacKay, president and CEO of AVROBIO. “Additionally, the first patient in the investigator-sponsored trial for cystinosis, now out one year, remains off both oral and eye drop cysteamine and we are thrilled to announce that a third patient has been dosed.

“As we move into the next stage of company growth, we’re expanding our lysosomal disorder pipeline with a new program for Gaucher disease type 3 and we plan to dose the first Hunter syndrome patient next year. We expect to be the first lentiviral gene therapy to the clinic across all six of these indications – and in some cases, the first to be in the clinic with an investigational gene therapy of any type. We believe the new data we’ve announced today help de-risk our portfolio which leverages the same lentiviral gene therapy approach across indications,” MacKay added. “With strong clinical trial enrollment momentum coming out of the COVID-19-related slowdown, we anticipate dosing, enrolling or consenting five patients across our clinical trials this quarter, and dosing a total of 30 patients cumulatively across our clinical programs by the end of 2021.”

Positive clinical data out as far as 3.5 years across a broad lysosomal disorder gene therapy pipeline

New clinical updates announced today include:

- **AVR-RD-02 for Gaucher disease type 1: Positive early reductions in plasma lyso-Gb1 and chitotriosidase activity at three months as compared to baseline, when Patient 1 was on ERT; additional positive trends observed across multiple other measures.**

  Three months post-gene therapy, the first patient dosed had a 22-percent reduction in the toxic metabolite plasma lyso-Gb1, a sensitive and clinically validated biomarker for Gaucher disease, compared to a baseline taken when she was stable on ERT, the current standard of care. Additionally, she had a 17-percent drop from her ERT baseline in plasma chitotriosidase, a biomarker of activated macrophages or “Gaucher cells” which lead to inflammation and severe organ damage. The vector copy number (VCN) at three months was 0.6 vcn/dg. Additionally, hemoglobin concentration and platelet counts, which are typically low in Gaucher disease patients, remained in the normal range three months after gene therapy. Patient 1 discontinued ERT one month before the gene therapy infusion and remains off ERT.

  At three months post-gene therapy, no unexpected safety events or trends have been identified in the trial, with no serious adverse events related to AVR-RD-02 reported in the first patient dosed as of the safety data cut-off date, Nov. 3, 2020.

- **AVR-RD-01 for Fabry disease: Potential accelerated approval strategy planning underway as clinical data across Phase 1 and Phase 2 trials continue to show positive and durable clinical activity and safety data.**

  With data from both trials showing consistently favorable results up to 3.5 years post-gene therapy, AVROBIO is in advanced planning of its strategy toward potential accelerated approval pathways. The company intends to submit its briefing book in 4Q 2020 to the U.S. Food and Drug Administration (FDA) with the goal to align on a potential accelerated approval strategy.

  The company reported durable and sustained response in enzyme activity, substrate levels and VCN across patients in both the Phase 1 and Phase 2 trials as of the data cut-off date, indicating successful engraftment of genetically modified cells and endogenous production of the functional enzyme needed to break down toxic substrate and metabolites in patients. Updated biomarker data on kidney function show generally stable estimated glomerular filtration rate (eGFR) in both Phase 1 and Phase 2 patients. Historically, people living with Fabry disease experience a progressive, faster-than-normal rate of decline in kidney function, as measured by eGFR, whether or not they are on ERT, the current standard of care. AVROBIO believes the stability in eGFR for patients in its clinical trials to be clinically significant and relevant.

  No unexpected safety events or trends have been identified in the trials as of the safety data cut-off date, Oct. 8, 2020. The eight serious adverse events reported in the two Fabry disease trials have been consistent with the conditioning regimen, stem cell mobilization, underlying disease or pre-existing conditions. Pre-existing low anti-AGA antibody titers have been detected in four patients in the Fabry Phase 1 trial and a transient low titer was observed but not detectable in subsequent measures in one patient in the Fabry Phase 2 trial.

- **AVR-RD-04 for cystinosis: Functional and clinical improvements for the first patient at 1 year; third patient in the trial dosed**

  The first patient dosed in the Phase 1/2 trial, now 12 months post-dosing, remains off both oral and eye drop cysteamine. Biopsy data showed a 56-percent decrease in the number of crystals in his skin, suggesting that the patient may now be producing his own functional cystinosin protein – which he was unable to do before receiving AVR-RD-04 – and that the protein is potentially preventing the toxic accumulation of cystine crystals. Images of the patient's cornea also showed a substantial decline in corneal crystals. His eGFR has been stabilizing post-infusion, though it is important to note that he had pre-existing, irreversible chronic kidney disease prior to trial enrollment. VCN has reached its therapeutic plateau, as expected, measuring 0.9 vcn/dg at 12-months post-dosing, mirroring trends seen in AVROBIO's other clinical programs. Patient 2 had a VCN of 2.2 vcn/dg at three months post-gene therapy, as of Oct. 13, 2020. A new patient has been dosed this month in the investigator-sponsored[1] study of AVR-RD-04 for cystinosis, marking the halfway point for enrollment with three patients dosed in total.

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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).*

No unexpected safety events or trends have been identified in the trial, with no serious adverse events reported as of the Nov. 2, 2020, safety data cut-off date.

Pioneering approach to personalized conditioning to leverage advantages of busulfan

The company also shared new data on the safety and tolerability profile of precision conditioning with busulfan prior to gene therapy administration. AVROBIO is pioneering a new approach called targeted concentration intervention (TCI) that enables precise dosing designed to optimize engraftment durability and head-to-toe reach of ex vivo lentiviral gene therapies. TCI aims to maximize the likelihood of engraftment while minimizing the risk of out-of-range side effects by targeting busulfan exposure to an area under the curve of 90 mg x hr/L over four days, called Bu90-TCI.

In AVROBIO's clinical trials to date, data suggest that side effects from its single-agent, single-cycle approach to Bu90-TCI conditioning may be predictable, manageable and transient. The side effects have tended to be mild to moderate in nature and typically presented one week after dosing and peak over three to four days before quickly subsiding. Unlike other conditioning agents, Bu90-TCI is lymphocyte sparing, meaning that important components of the adaptive immune system, B and T cells, are expected to be minimally affected.

Strategic pipeline expansion into relentlessly progressive lysosomal disorders

AVROBIO announced the addition of Gaucher disease type 3 to its pipeline, following the recent addition of Hunter syndrome, which is planned to enter the clinic next year. Together with the existing program in Pompe disease, these make up AVROBIO's second wave of clinical programs focused on life-threatening lysosomal disorders, with the goals of preventing the central nervous system and systemic deterioration that make lysosomal disorders so devastating, normalizing lifespan and lifting the burden of chronic treatment with ERT. New preclinical data suggest that AVROBIO's proprietary tagging technology, part of its industry-leading plato® gene therapy platform toolbox, further enhances the potential of its investigational gene therapies in these disorders.

“We believe that all six of our pipeline programs share tremendous synergies in clinical development, manufacturing, regulatory processes and commercialization. This second wave of programs will evaluate our promising investigational therapies in diseases with high unmet medical need for patients and families,” said Chris Mason, M.D., Ph.D., chief scientific officer at AVROBIO. “We believe the opportunity we have to potentially prevent patients, especially children, from developing the disabilities that would otherwise result from their inherited genetic code – to perhaps give them the possibility of a full and healthy life – is humbling. That is our purpose; it drives all of us at AVROBIO every day.”

Preclinical updates include:

- **AVR-RD-05 for Hunter syndrome: Normalization of multiple biomarkers in mouse model of the disease**

  The presented data showed that a lentiviral gene therapy incorporating an ApoE2 tag used in AVR-RD-05 and in-licensed from the University of Manchester, U.K., substantially reduced substrate accumulation and neuroinflammation in mouse models of Hunter syndrome to levels seen in normal mice. The presence of the tag significantly improved performance across multiple metrics in preclinical models, including normalization of skeletal features such as the cheekbone dimensions and the width of the humerus and femur bones. Patient dosing is planned to begin in 2H 2021 in an investigator-sponsored trial with the University of Manchester. The company is exploring regulatory options, including expedited development programs, to advance the product for use in neuronopathic patients, the most severe form of the disease.

- **AVR-RD-06 for Gaucher disease type 3: New program leveraging the same vector as AVR-RD-02 for Gaucher disease type 1**

  The disease burden for patients with Gaucher disease type 3 includes significant neurological deterioration, which AVROBIO believes AVR-RD-06 has the potential to address by replacing diseased microglia and macrophages, or “Gaucher cells,” with genetically modified cells throughout the body and brain.

- **AVR-RD-03 for Pompe disease: Preclinical data show normalization of substrate levels in multiple hard-to-reach organs**

  The presented data showed that a lentiviral gene therapy incorporating a proprietary Glycosylation-Independent Lysosomal Targeting (GILT) tag used in AVR-RD-03 and in-licensed from BioMarin, reduced toxic glycogen accumulation by 97 to 100 percent in tissues including the brain, spinal cord, heart and diaphragm, and by more than 85 percent in skeletal muscle in a mouse model of the most severe form of the disease, classic infantile-onset Pompe disease. Four to eight months after dosing, substrate levels in multiple tissues of the mice treated with the tagged lentiviral gene therapy were nearly indistinguishable from normal mice. AVROBIO believes that these exciting results could only be achieved with the GILT tag to drive uptake into hard-to-reach tissues. The company is exploring options to rapidly advance AVR-RD-03 into the clinic for treatment of classic infantile-onset Pompe disease.

End-to-end plato® platform ready to enable global commercialization

AVROBIO also presented data on its industry-leading plato® platform highlighting advances in chemistry, manufacturing and controls (CMC) to prepare for planned upcoming trials and potential global commercialization.

The optimized processes embedded in plato are designed to enable robust product characterization and efficient production of potent, consistent drug product on two continents, with a third site slated to become operational in Europe in 2021. New advances include:

- **Development of a universal VCN assay that may be leveraged across the portfolio**: AVROBIO believes that this universal assay, intended to be transferred to multiple regulatory jurisdictions, represents a significant advance in the industry. It is designed to build a strong foundation to support future biologics license applications.
- **Advances in next-generation analytics to potentially enable deep product characterization**: AVROBIO leads in single-cell analytics and whole transcriptome profiling, such as characterization of tens of thousands of single cells in the apheresis starting material used to make the drug product.
- **Implementation of global infrastructure built to scale production to meet commercial demands**: plato is built with efficiency, scalability and speed in mind, from large-scale plasmid and vector manufacturing to automated drug product production to cryopreservation.

R&D Day webcast information

A live webcast of Virtual R&D Day and accompanying slides will be available under “Events and Presentations” in the Investors section of the company’s website at www.avrobio.com. An archived webcast recording of the event will be available on the website for approximately 30 days.

About AVROBIO

Our vision is to bring personalized gene therapy to the world. We aim to prevent, halt or reverse disease throughout the body with a single dose of gene therapy designed to drive durable expression of functional protein, even in hard-to-reach tissues and organs including the brain, muscle and bone. Our ex vivo lentiviral gene therapy pipeline includes clinical programs in Fabry disease, Gaucher disease type 1 and cystinosis, as well as preclinical programs in Hunter syndrome, Gaucher disease type 3 and Pompe disease. AVROBIO is powered by its industry leading plato® gene therapy platform, our foundation designed to deliver 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, results of preclinical studies, the design, commencement, enrollment and timing of ongoing or planned clinical trials, clinical trial results, product approvals and regulatory pathways, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, timing and likelihood of success, and the expected benefits and results of our implementation of the plato platform in our clinical trials and gene therapy programs, including the use of a personalized and ultra-precision busulfan conditioning regimen. 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 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 enrollment and development timelines 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 materially and adversely 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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