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): January 4, 2022

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 January 4, 2022, AVROBIO, Inc. issued a press release titled “AVROBIO Reprioritizes Pipeline Programs” and updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the press release and corporate presentation are filed as Exhibits 99.1 and 99.2, respectively, 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	AVROBIO, Inc. press release, dated January 4, 2022.
99.2	AVROBIO, Inc. slide presentation, dated January 2022.
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBR

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: January 4, 2022

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

Exhibit 99.1

AVROBIO Reprioritizes Pipeline Programs

Fabry disease program to be deprioritized, shifting focus to other clinical-stage programs in lysosomal disorder pipeline

Data updates for cystinosis and Gaucher disease type 1 programs planned for 1H 2022, with regulatory interactions anticipated across multiple programs in 2022

Cash runway to be extended into first quarter of 2024

CAMBRIDGE, Mass.—(BUSINESS WIRE)—Jan. 4, 2022—AVROBIO, Inc. (Nasdaq: AVRO), a leading clinical-stage gene therapy company with a shared purpose to free people from a lifetime of genetic disease, today announced that it is shifting its portfolio priorities to focus on other clinical-stage programs and extending its cash runway into the first quarter of 2024. The company is deprioritizing its Fabry disease program due to several factors, including new clinical data showing variable engraftment patterns from the five most recently dosed Phase 2 FAB-GT patients which would significantly extend the program's development timeline, as well as an increasingly challenging market and regulatory environment for Fabry disease.

"Following steady progress in 2021, we have reset our corporate priorities and will extend our cash runway to strengthen our ability to deliver on the promise of our gene therapy programs," said Geoff MacKay, president and CEO of AVROBIO. "Powered by our proprietary plato® gene therapy platform, we will focus our efforts on moving value driving clinical-stage programs forward in 2022, with data updates expected for our cystinosis and Gaucher disease type 1 programs, as well as regulatory interactions anticipated across multiple programs in our pipeline.

"Previously reported data from 13 patients treated across our three clinical-stage programs have shown durable engraftment out 9 to 54 months. It is the new data from the five most recently dosed Phase 2 FAB-GT patients that are discordant with these other data and show variable engraftment. In addition, the last 12 months have presented multiple challenging market and regulatory dynamics for our Fabry disease program, which would now be exacerbated by a meaningfully extended development timeline," said MacKay. "We're fully aware of the impact this difficult decision has on the patients and families whom we have had the privilege to get to know over the years, but we believe deprioritizing and halting enrollment in our Fabry disease program is the right step forward for AVROBIO and preserves our ability to continue developing therapies with the potential to address urgent unmet needs in the lysosomal disorder community."

New data from Phase 2 FAB-GT clinical trial show variable engraftment

The aggregated data from the five most recently dosed FAB-GT patients showed variable engraftment patterns. Data from three of the five patients showed both a reduction to near baseline levels in alpha-galactosidase A (AGA) enzyme activity in leukocytes and plasma, and a reduction in vector copy number (VCN) in whole blood, potentially suggesting resistance to persistent engraftment of the genetically modified cells observed at three to nine months post infusion of AVR-RD-01. (See data slides here)

Based on its investigation, the company believes, due to the large degree of heterogeneity in Fabry disease, that in some cases there may be intrinsic resistance to engraftment related to the unique underlying pathophysiology of untreated Fabry disease, potentially caused by the persistently stressed vascular endothelium. The company also has reviewed potential procedure-related factors and conditioning parameters, including the possible impact, in the context of untreated Fabry disease, of a previous clinical trial protocol amendment for the five recently dosed patients which prolonged the conditioning agent washout period by up to 48 hours.

“Importantly, the drug product specifications for these five patients met all release criteria,” said MacKay. “Additionally, these variable engraftment patterns have not been observed to date in data from the other nine Fabry disease patients previously dosed in the Phase 1 trial and under the prior protocol amendments in the FAB-GT trial, or in data from any patients in our other ongoing clinical trials.”

Safety data from all nine adult patients dosed in the Phase 2 FAB-GT trial and the five adult patients dosed in the investigator-sponsored Phase 1 trial show no adverse events (AEs) or serious adverse events (SAEs) related to drug product AVR-RD-01, as of the most recent data cut-off date.

The company will stop enrollment for the FAB-GT clinical trial and continue monitoring the previously dosed patients for a total of 15 years as required by regulators.

Updated 2022 program guidance

Anticipated pipeline milestones include:

- AVR-RD-04 for cystinosis: Provide an update at the WORLD*Symposium*™ 2022 on collaborator-sponsored Phase 1/2 clinical trial of AVR-RD-04 (CTNS-RD-04),[i] and plan to engage with regulatory agencies on a planned Phase 2 company-sponsored clinical trial
- AVROBIO’s Gaucher disease programs:
  - AVR-RD-02 for Gaucher disease type 1: Provide a clinical update in the first half of 2022
  - AVR-RD-06 for Gaucher disease type 3: Engage with regulatory agencies on a planned Phase 2/3 clinical development strategy for AVR-RD-06; planning to initiate a clinical trial in 2023
- AVR-RD-05 for Hunter syndrome: Collaborators at the University of Manchester plan to initiate a collaborator-sponsored Phase 1/2 clinical trial in 2023

- AVR-RD-03 for Pompe disease: Engage with regulatory agencies on the clinical development strategy for AVR-RD-03; planning to initiate a clinical trial in 2023
- plato® platform: Continue research collaborations to evaluate the potential use of monoclonal antibody conditioning agents in Gaucher disease type 1 trial

As of Sept. 30, 2021, the company had $201 million in cash and cash equivalents. As a result of the pipeline reprioritization, the company expects to extend its cash runway into the first quarter of 2024.

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 therapeutic protein, even in hard-to-reach tissues and organs including brain, muscle and bone. AVROBIO's pipeline is powered by our industry-leading plato® gene therapy platform, our foundation designed to deliver gene therapy worldwide. It includes clinical programs in cystinosis and Gaucher disease type 1, as well as preclinical programs in Gaucher disease type 3, Hunter syndrome and Pompe disease. 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 plans and expectations for reprioritizing our program pipeline, including the deprioritization of our Fabry disease clinical program, 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 regulatory interactions, anticipated benefits of our gene therapy platform including potential impact on our commercialization activities, timing and likelihood of success, the expected benefits and results of our implementation of the plato® platform in our clinical trials and gene therapy programs, the potential use of monoclonal antibody conditioning agents, and our financial position and cash runway expectations. 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, risks related to regulatory interactions and intended development pathways 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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[i] 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).

Exhibit 99.

Disclaimer

This presentation has been prepared by AVROBIO, Inc. ("AVROBIO") for informational purposes only and not for any other purpose.

This presentation may contain forward-looking 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 plans and expectations for reprioritizing our program pipeline, including the deprioritization of our Fabry disease clinical program; our business strategy for and the potential therapeutic benefits of our current and prospective product candidates; the design, commencement, enrollment and timing of ongoing or planned clinical trials and regulatory pathways; our plans and expectations with respect to the development of our clinical and preclinical product candidates, including timing, design and initiation of our potential clinical and registration trials and anticipated interactions with regulatory agencies; the timing of anticipated clinical and regulatory updates; the timing of patient recruitment and enrollment activities, clinical trial results, and product approvals; the timing and results of our ongoing preclinical studies; the anticipated benefits of our gene therapy platform including the potential impact on our commercialization activities, timing and likelihood of success; the expected benefits and results of our manufacturing technology, including the implementation of our plato® platform in our clinical trials and gene therapy programs; the potential use of monoclonal antibody conditioning agents; the expected safety profile of our investigational gene therapies; and our financial position and cash runway expectations. Any such statements in this presentation that are not statements of historical fact may be deemed to be forward-looking statements.

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 that regulatory agencies may disagree with our anticipated development approach for any one or more of our product candidates; 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, including our use of busulfan as a conditioning agent or potential use of monoclonal antibody conditioning agents, 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 ongoing COVID-19 pandemic 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, 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.

Note regarding trademarks: plato® is a registered trademark of AVROBIO. Other trademarks referenced in this presentation are the property of their respective owners.

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Today's press release

- **Deprioritizing Fabry disease program and shifting focus to other clinical-stage programs in lysosomal disorder pipeline**
  - New data from five most recently dosed patients in Phase 2 FAB-GT trial show variable engraftment
  - Decision driven by several factors, including significantly extended development timeline and increasingly challenging market and regulatory environment for Fabry disease
  - Based on our investigation, we believe due to large degree of heterogeneity in Fabry disease, in some cases there may be intrinsic resistance to engraftment related to the unique underlying pathophysiology of untreated Fabry disease, potentially caused by persistently stressed vascular endothelium
  - Also reviewed potential procedure-related factors and conditioning parameters, including possible impact, in the context of untreated Fabry disease, of previous clinical trial protocol amendment for five most recently dosed patients which prolonged the conditioning agent washout period by up to 48 hours
  - Drug product specifications for all patients met all release criteria
- **No observed read-through to other clinical trials to date**
  - Data from 13 patients previously reported have shown durable engraftment out 9 to 54 months
    - 4 previously dosed patients in FAB-GT trial
    - 5 dosed in Phase 1 Fabry disease trial
    - 3 dosed in Phase 1/2 cystinosis trial
    - 1 dosed in Phase 1/2 Gaucher disease type 1 trial
- **Cash runway to be extended into Q1 2024**
- **Multiple data and regulatory updates expected in 2022**

Two AVR-RD-01 Fabry clinical trials

14 patients dosed across Phase 1 and 2

PHASE 1

Investigator-Sponsored Trial*

FULLY ENROLLED

OBJECTIVES	PATIENTS
• Safety and tolerability • Preliminary efficacy	• n = 5 patients • 18 – 59 year-old males • On ERT >6 months prior to enrollment

PHASE 2

AVROBIO FAB-GT Trial **

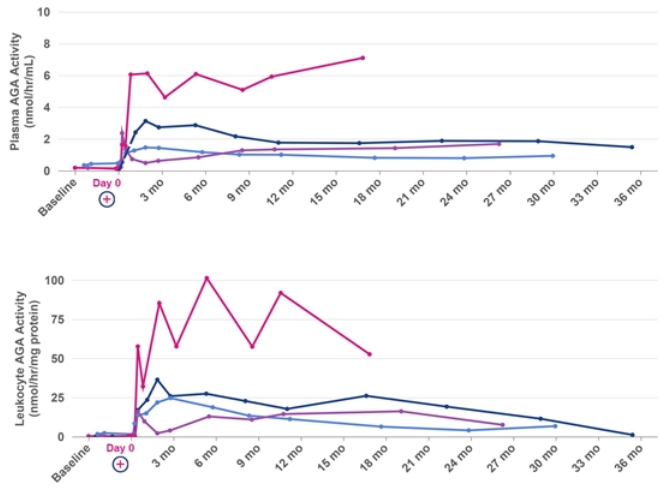
OBJECTIVES	PATIENTS
• Safety and tolerability • Efficacy	• n = 8-12 patients (9 dosed to-date) • 16 – 50 year-old males • Treatment naïve

** Sponsored by FACTs team (Fabry Disease Clinical Research and Therapeutics) in Canada*
*** FAB-GT f/k/a FAB-201*

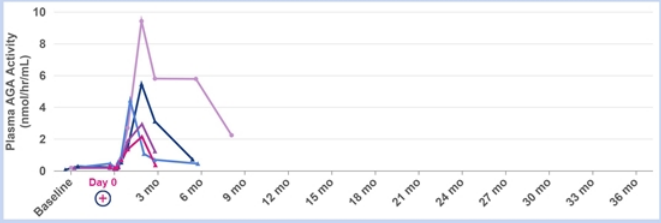
Phase 2 FAB-GT

Reduction to near baseline in AGA enzyme activity in 3 of 5 most recently dosed patients 3-9 months post-gene therapy

Patients 1-4



Patients 5-9



AGA leukocyte normal reference range between 24-56 nmoles/hr/mg protein; AGA plasma normal reference range is 5.1-9.2 nmoles/hr/ml

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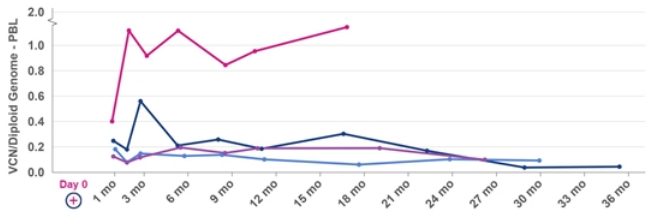
Phase 2 FAB-GT

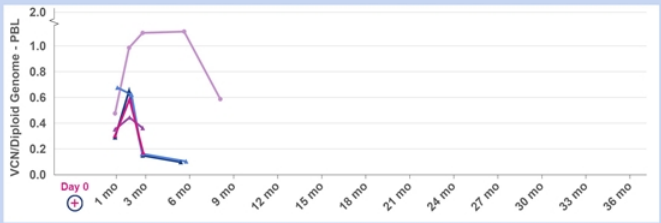
Reduction in whole blood VCN in most recently dosed patients 3-9 months post-gene therapy

Patients 1-4



Drug Product VCN/dg
Patient 1: 0.7
Patient 2: 0.53
Patient 3: 1.36
Patient 4: 1.56

Patients 5-9



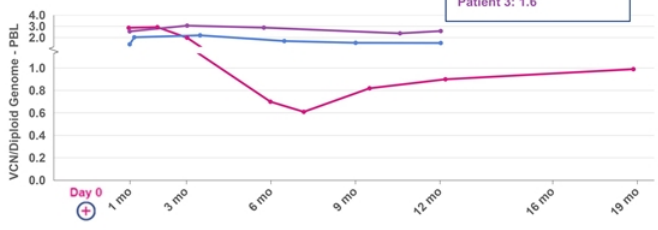
Drug Product VCN/dg
Patient 5: 1.0
Patient 6: 0.9
Patient 7: 1.1
Patient 8: 0.8
Patient 9: 0.5

101-101 (Pt. 1) 102-102 (Pt. 2) 101-102 (Pt. 3) 102-104 (Pt. 4) 101-104 (Pt. 5)
101-105 (Pt. 6) 102-105 (Pt. 7) 101-107 (Pt. 8) 101-106 (Pt. 9)

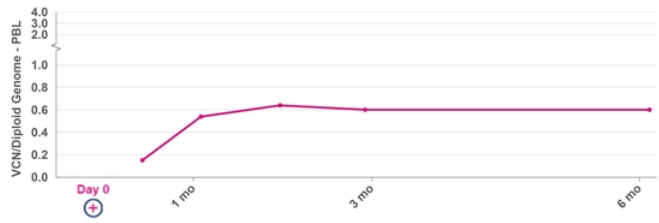
AVROBIO plato

Data from 13* patients previously reported have shown durable engraftment out 9 to 54 months

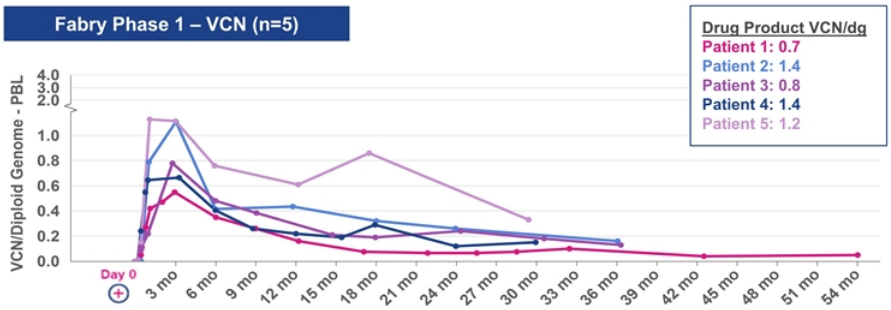
Cystinosis – VCN (n=3)



Gaucher – VCN (n=1)



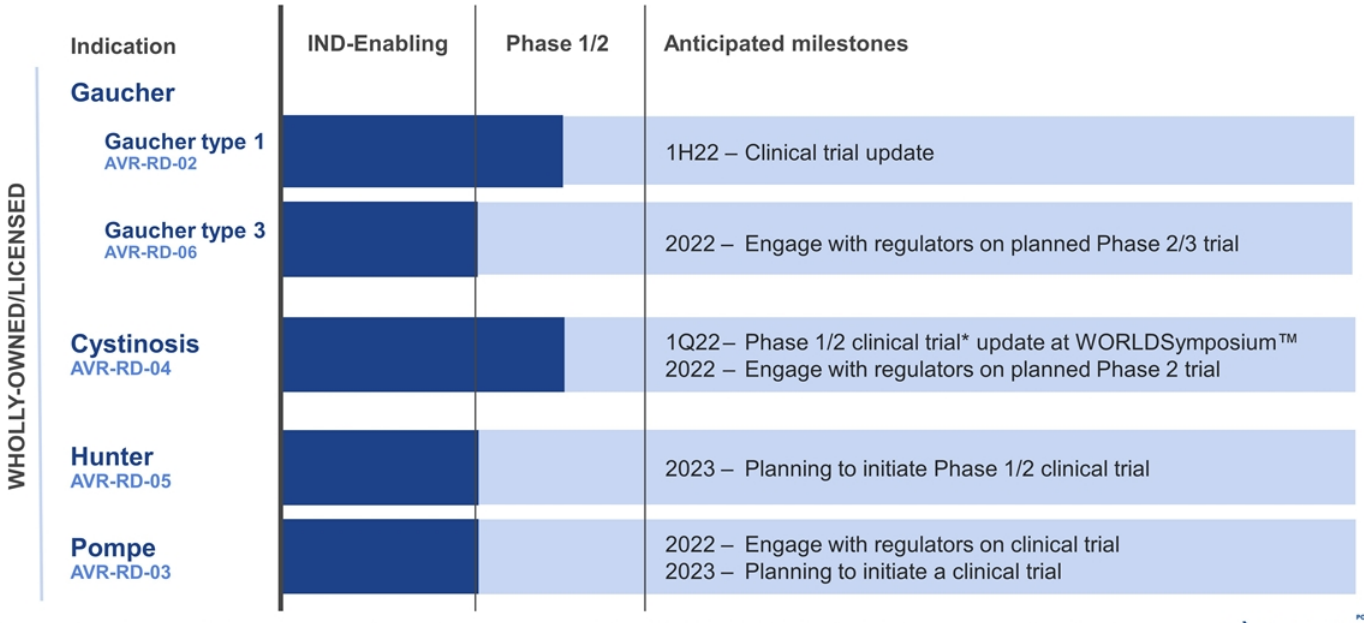
Fabry Phase 1 – VCN (n=5)



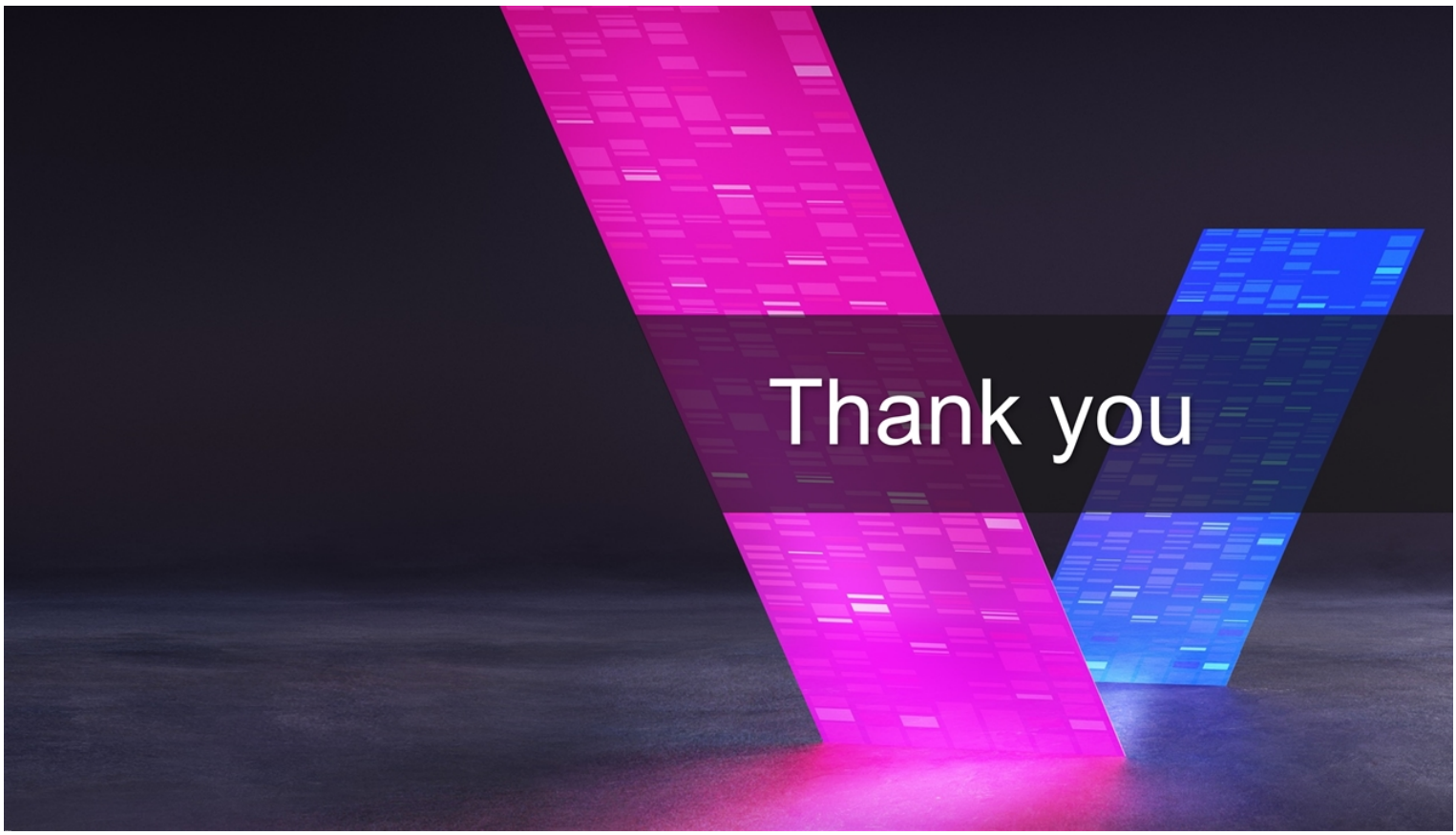
*VCN: Vector Copy Number; PBL: Peripheral Blood Leukocytes; dg: Diploid Genome; *VCN for FAB-GT patients 1-4 provided on previous slide*

Leading lysosomal disorder gene therapy pipeline

Anticipated data and regulatory milestones



*Planned regulatory milestones subject to regulatory agency clearance; * 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).*


Thank you

Appendix

Busulfan washout period and cumulative AUCs

Longer washout period in 5 most recently dosed patients

PATIENT	WASHOUT PERIOD (HOURS)	CUMULATIVE AUC (TARGET: 90 MG.HR/L CUMULATIVE)
Patient 1	Melphalan conditioning regimen (~24 hours)	N/A
Patient 2		
Patient 3		
Patient 4	25	91.1
Patient 5	70	84.5
Patient 6	67	97.6
Patient 7	70	90.7
Patient 8	70	90.3
Patient 9	69	96.1