AVROBIO

Freedom from a lifetime of disease

Pre-Approval Commercialization Workshop

Clinical Path to Commercialization: Manufacturing Challenges

Kim Warren, Ph.D

ASGCT, 28 April 2019

Disclaimer

This presentation has been prepared by AVROBIO, Inc. ("AVROBIO") for informational purposes only and not for any other purpose. Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources and AVROBIO's own internal estimates and research. While AVROBIO believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and AVROBIO makes no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. While AVROBIO believes its internal research is reliable, such research has not been verified by any independent source.

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 such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts", "goal," "intends," "may" "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. These forward-looking statements include, without limitation, statements regarding our business strategy, prospective products and goals, the therapeutic potential of our product candidates, the design, enrollment and timing of ongoing or planned clinical trials, clinical trial results, product approvals and regulatory pathways, potential regulatory approvals and the timing thereof, anticipated benefits of our gene therapy platform, timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated products, and the market opportunity for our product candidates. 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 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 realize the intended benefits our gene therapy 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, 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2018, 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.

AVROBIO

AVR-RD-01 **Fabry clinical trials**

7 patients dosed across Phases 1 and 2

PHASE 1 Investigator-Sponsored Trial*	**PHASE 2** AVRO – FAB-201 Trial
Patients **n = 5 (fully enrolled)** **On ERT > 6 months prior to enrollment** **18-50 year-old males**	**Patients** **n = 8-12** **ERT-naive** **≥ 16 year-old males**
Key Objective Safety	**Key Objectives** Safety and efficacy

AVROBIO

** Sponsored by FACTS team (Fabry disease Clinical research and Therapeutics) in Canada*

Goals for gene therapy in **Fabry disease**

TO PREVENT OR IMPROVE:

Kidney function
Unmet needs: proteinuria, polyuria, kidney failure

Cardiac function
Unmet needs: left ventricular hypertrophy, fibrosis, heart failure

Neuropathic pain
Unmet needs: pain and burning sensations in hands and feet, pain crises

Everyday burden of illness, and life expectancy
Unmet needs: fatigue, inability to sweat, joint pain, abdominal pain, diarrhea, vomiting, cloudy vision, hearing loss, tinnitus, rash, angiokeratomas, biweekly infusions, shortened lifespan

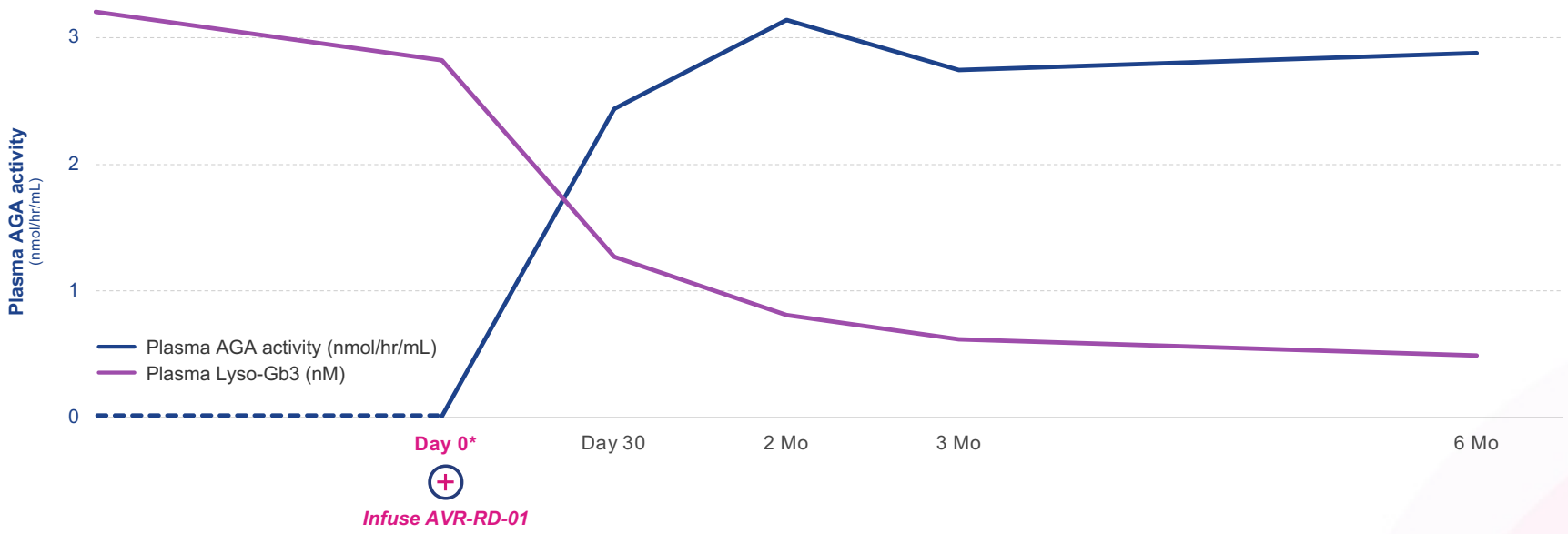
CNS complications
Unmet needs: TIA/stroke, depression, mild cognitive deficiency, white matter hyperintensities

Sources: Wanner C et al, Med Genetics and Metab, 2018; Burlina A, JIEMS, 2016

AVROBIO

FAB-201: AVROBIO Phase 2 study in **Treatment-Naïve Fabry patients**

Patient #1: Substantial increase in AGA enzyme activity and 85% reduction in plasma lyso-Gb3 levels observed within 6 months



AVROBIO

** Dotted line represents AGA activity measured in serum*

FAB-201 SUMMARY

PATIENT FAB-201-1 at 6 months

FAB-201: Phase 2 in treatment-naïve Fabry patients

- Substantial enzyme increase
- Associated with substrate reduction
- Generally well tolerated
- Awaiting long-term follow-up

AVROBIO

Important Considerations

For developing a manufacturing process

Streamlined setup is valuable for rare diseases

- Simple and straightforward: Reduced training
- No open steps: Low sterility risk
- Short
- Limit timing issues
- Second source suppliers
- Platform process: same or similar steps across indications, equipment, materials, testing and regulatory approach

AVROBIO

plato™

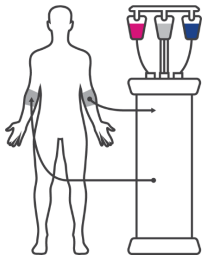
AVROBIO's foundation for worldwide commercialization

- A **vector system** and cell **manufacturing solution** designed to support commercialization
- **Automated, closed manufacturing system** for CD34+ gene therapy
- Designed to safely deliver **long-term efficacy** and **durability**

plato™
Gene therapy.
Evolved.

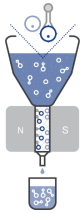
plato™ AVROBIO

Closed, automated system



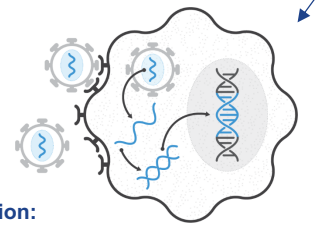
Mobilization & Apheresis:
Patient hematopoietic stem cells (HSCs) collected by apheresis following mobilization with G-CSF + plerixafor

Patient Consent and Screening



Cell Separation & Culture:
CD34+ HSCs selected using magnetic beads and put into culture overnight with priming growth factors

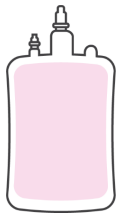
Lentiviral Vector Production



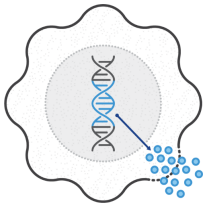
Transduction:
HSCs transduced with lentiviral vector carrying target gene, and cultured overnight

One Platform
applied across
AVROBIO portfolio

Harvesting & Cryopreservation:
HSCs harvested and cryopreserved, shipped to clinical site once release testing is completed



Drug Product Testing



Gene Therapy Administration:
HSCs are infused back into patient, where they home to the bone marrow, engraft and produce daughter cells expressing the target gene and produce functional enzyme

Patient Monitoring

Conditioning:
Patient undergoes conditioning regimen with therapeutic drug monitoring to clear space in the bone marrow

plato™ overcomes historical bottlenecks to **enable commercialization**

Expanded Scale

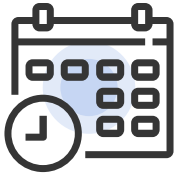
Potential to reach thousands of patients per year

Broader Reach

Portable platform for flexible global production using low grade clean rooms

High Quality

Automated, closed system designed to improve quality and consistency



Longer Shelf-Life

Cryopreservation simplifies logistics and patient scheduling

Lower Costs

Efficiencies in vector design / scalable cell and vector production

Thank you

AVROBIO

plato™
Gene therapy.
Evolved.