Summary

This opportunity offers a visionary CEO the chance to lead a potentially breakthrough pharmaceutical therapy in a high unmet need area, supported by foundational science, a pioneering bioenergetic approach, strong IP, and an expert team. The role will directly impact millions of Alzheimer's patients and their families through innovative drug development.

Background

Aerobyx, LLC was formed in 2017 to develop a new class of drugs called bioenergetic medicines. Bioenergetics is the science of the flow and transformation of energy within living organisms. Bioenergetic medicine targets failures and impairments to energy metabolism in cells, such as mitochondrial dysfunction, with compounds designed to repair and restore these processes.

Alzheimer's Disease (AD) is a devastating and progressive neurodegenerative disorder with no current cure or effective disease-modifying treatment. It causes more deaths annually than breast and prostate cancers combined. Currently, over 7 million Americans live with AD, and this number is projected to rise dramatically. Growing evidence highlights mitochondrial dysfunction and impaired brain energy metabolism as key early drivers of AD pathology. Aerobyx's lead compound, ARBX-225, is designed to enhance mitochondrial function and neuron energy metabolism by combining two compounds that pilot studies report associate with either cognitive benefits or brain bioenergetic target engagement in AD subjects.

The company has demonstrated promising preclinical data in mice supporting pharmacokinetics, pharmacodynamics, and target engagement. IP protection includes a granted composition of matter patent for the drug substance and two continuation patent applications. The patents are owned by the University of Kansas and controlled by Aerobyx, LLC via an Option for an Exclusive License. Aerobyx operates as a lean virtual organization with experienced scientific and pharmaceutical leaders, including co-founder and CSO Dr. Russell Swerdlow, a globally recognized expert in mitochondrial medicine, Distinguished Professor and current Director of the Alzheimer's Disease Research Center at the University of Kansas and co-founder and COO Laird Forrest, a Professor of Pharmaceutical Chemistry at the University of Kansas. Support publications include:

- Swerdlow RH. Bioenergetic Medicine. BJP 2014;171:1854-1869. URL: https://pmc.ncbi.nlm.nih.gov/articles/PMC3976609/
- Wilkins HM, Koppel S, Carl SM, Ramanujan S, Weidling I, Michaelis ML, Michaelis EK, Swerdlow RH. Oxaloacetate Enhances Neuronal Cell Bioenergetic Fluxes and Infrastructure. J Neurochem 2016;137:76-87. https://pmc.ncbi.nlm.nih.gov/articles/PMC5482267/
- E L, Lu J, Selfridge JE, Burns JM, Swerdlow RH. Lactate administration reproduces specific brain and liver exercise-related changes. J Neurochem 2013;127:91-100. URL: https://pmc.ncbi.nlm.nih.gov/articles/PMC4276250/
- Wilkins HM, Harris JL, Carl SM, E L, Lu J, Selfridge JE, Roy N, Hutfles L, Koppel S,

Morris J, Burns JM, Michaelis ML, Michaelis EK, Brooks WM, Swerdlow RH. Oxaloacetate activates brain mitochondrial biogenesis, enhances the insulin pathway, reduces inflammation, and stimulates neurogenesis. Hum Mol Genet 2014;23:6528-6541. https://pmc.ncbi.nlm.nih.gov/articles/PMC4271074/

- Selfridge JE, Wilkins HM, E L, Carl SM, Koppel S, Funk E, Fields T, Lu J, Tang EP, Slawson C, Wang WF, Zhu H, Swerdlow RH. Effect of one month duration ketogenic and non-ketogenic high fat diets on mouse brain bioenergetic infrastructure. J Bioenergetics Biomembranes 2015;47:1-11. https://pmc.ncbi.nlm.nih.gov/articles/PMC4320989/
- Swerdlow RH, Lyons KE, Khosla SK, Nashatizadeh M, Pahwa R. A pilot Study of oxaloacetate 100 mg capsules in Parkinson's disease patients. JPA 2016;3:4 https://pdfs.semanticscholar.org/7003/5129fc683f3f06d6a82b1501d417abf5d09c.pdf
- Taylor MK, Sullivan DK, Mahnken JD, Burns JM, Swerdlow RH. Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease. Alz Dem TRCI 2018;4:28-36. https://pmc.ncbi.nlm.nih.gov/articles/PMC6021549/
- Vidoni ED, Choi IY, Lee P, Reed G, Zhang N, Pleen J, Mahnken JD, Clutton J, Becker A, Sherry E, Bothwell R, Anderson H, Harris RA, Brooks W, Wilkins HM, Mosconi L, Burns JM, Swerdlow RH. Safety and target engagement profile of two oxaloacetate doses in Alzheimer's patients. Alz Dement 2020;17:7-17. https://pmc.ncbi.nlm.nih.gov/articles/PMC8084114/
- Swerdlow RH, de Leon MJ, Marcus DL. Betahydroxybutyrate Consumption in Autopsy Brain Tissue from Alzheimer's Disease Subjects. JAD Reports 2021;5:135-141. https://pmc.ncbi.nlm.nih.gov/articles/PMC7990458/
- Koppel SJ, Wilkins HM, Weidling IW, Wang X, Menta BW, Swerdlow RH.
- β-hydroxybutyrate Preferentially Enhances Neuron Over Astrocyte Respiration While Signaling Cellular Quiescence. Mitochondrion 2023:68:125-137. https://pmc.ncbi.nlm.nih.gov/articles/PMC9805520/
- Swerdlow RH. The Alzheimer's Disease Mitochondrial Cascade Hypothesis: A Current Overview. JAD 2023;92:751-768. DOI: 10.3233/JAD-221286 https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC3962811&blobtype=pdf

In its seven years of operation, approximately $5.6M of non-dilutive funding has been invested to develop the body of evidence supporting the likelihood of success for ARBX-225. This includes:

ACTIVITY / STUDY DESCRIPTION	***SPENDING / INVESTMENT***
Ralph Solarski (CEO) – labor/time	$60,000
Russ Swerdlow (CSO) – labor/time	$120,000
Laird Forrest (COO) – labor/time	$120,000
Pharmacokinetics of Oxaloacetate (POX) KUMC Frontiers/KUMC Neurology Zeigler Award Aims: Determine human oxaloacetate pharmakokinetics	$20,000
Oxaloacetate's Brain Effects	$151,000

ACTIVITY / STUDY DESCRIPTION	*SPENDING / INVESTMENT*
R03 NS077852 NIH/NINDS Aims: Determine how oxaloacetate affects brain bioenergetic pathways	
Trial of Oxaloacetate in Alzheimer's Disease (TOAD) Trial Alzheimer's Association PCTR-15-330495 Aims: Assess tolerability and biomarker modification of ascending oxaloacetate doses in AD subjects	$570,000
Ketone Body-Based Interventions for Alzheimer's Prevention and Therapy Stop Alzheimer's Now Foundation Aims: Test how different types of ketosis induction influence brain metabolism	$100,000
Kansas University Frontiers-IAMI Pharmacokinetic Studies of a Novel Bioenergetic Medicine Ester Aims: Obtain animal pharmacokinetic data on a novel bioenergetic medicine ester	$50,000
Bioenergetic Manipulation for the Treatment of Alzheimer's Disease Kansas Board of Regents Experimental Program to Stimulate Competitive Research Aims: Synthesize and validate novel compounds that can enhance brain energy metabolism	$100,000
R43AG060817 Targeting bioenergetic flux for Alzheimer's disease management Aims: Advance the development of compounds that enhance brain bioenergetic fluxes	$225,000
R01AG060733 Validation and Mechanistic Interrogation of Metabolism Targeting for AD Aims: (1) Assess cognitive effects of a ketogenic diet cognition in Alzheimer's participants in a randomized trial, (2) Determine how the intervention affects bioenergetic, inflammatory, and lipid biology	$3,500,000
R21AG070466 Mitochondria Targeting for Alzheimer's Disease Aims: This project develops bioenergetic enhancing drugs for the treatment of Alzheimer's disease	$596,000

ARBX-225 DEVELOPMENT PLAN

Stage 1 – Concept Definition / Invention (Completed)

Stage 2 – Formulation and Proof of Concept (Current – will require fundraising)

- Formulation development (drug substance and drug product scaleup), characterization, GMP manufacturing process development
- Batch/production for GLP animal studies
- 2 animal studies: 1) preliminary Tox; 2) efficacy in an AD mouse model

Stage 3 – Pre-IND, IND and Phase 1 (based upon positive results in Stage 2, will require second fundraising effort)

- Pre-IND submission (including formal Tox plan, Clinical Plan and cGMP plan to get FDA's approval for the approaches)
- Tox Studies (under GLP)
- Initial cGMP production for Ph I study
- Clinical Plan (Ph I – Ph III at high level, including detailed Ph I clinical trial plan)
- IND
- Phase I study

Stage 4 – Phase 2 Clinical Study (based upon positive results from Stage 3, will require third fundraising effort – or potential sale/license to a Pharma company at this point)

Stage 5 – Phase 3 Clinical Study (based upon positive results from Stage 4, will require fourth fundraising effort – or potential sale/license to a Pharma company at this point)

Stage 6 – NDA Submission and Commercialization

Key Roles and Responsibilities for CEO

The incoming CEO will be pivotal in guiding ARBX-225 along the development path to commercialization.

- Develop and execute a detailed development plan for ARBX-225, including the timeline, key milestones and budget.
- Assemble and lead a team of experts in pharmaceutical formulation development, preclinical development, clinical development, regulatory affairs, CMC, and other functions as needed. (The CEO will determine which functions should be managed by contractors, firms, employees, etc.).
- Establish strategic partnerships with CDMOs, CROs and other organizations necessary to execute the development plan.
- Drive fundraising efforts across multiple rounds aligned with the development milestones.
- Lead/direct preclinical and clinical development programs
- Lead/direct regulatory interactions with US FDA and other global regulatory bodies, as appropriate.
- Lead/direct business development, investor communications, and licensing negotiations.

CEO Profile

The ideal CEO candidate will:

- Have extensive experience leading drug development startups, preferably in CNS, neurology, or neurodegenerative disease sectors.
- Possess deep knowledge of formulation development, clinical trial execution, and FDA regulatory processes for novel small molecules.
- Demonstrate a track record of successful fundraising, investor relations, and strategic partnership cultivation.
- Be capable of assembling a high-level leadership team across scientific, regulatory, manufacturing, and clinical domains in a virtual organization model.
- Exhibit passion for pioneering new therapeutic modalities with potential to transform treatment of Alzheimer's and related diseases.
- Be committed to a long-term vision to shepherd ARBX-225 through its decade-long development journey to market.
- Have excellent communication and collaborative leadership skills to engage with stakeholders from academia, industry, government, and patient advocacy groups.

Compensation and Support

This position will initially be structured as an equity-only role. Salary and benefits will be introduced as the company secures capital through planned funding rounds. The compensation framework reflects the early-stage nature of the venture while aligning leadership incentives with long-term enterprise growth.

The CEO will receive comprehensive support from the experienced founding team, the former CEO, and institutional partners at the University of Kansas. Dr. Russell Swerdlow, a globally recognized expert in mitochondrial medicine, will provide medical and scientific expertise. Dr. Laird Forrest will contribute expertise in pharmaceutical formulation and intellectual property strategy. Former CEO Ralph Solarski brings over forty years of cross-industry business experience, including the successful development and licensing of a pharmaceutical combination product.

Additionally, the company benefits from its affiliation with university-based resources such as the KU Innovation Park, which offers facilities, infrastructure, and commercialization support. The Oread Angel Network also represents a potential strategic partner for early-stage investment and advisory engagement.