Repurposing AMLEXANOX

A Potential Readthrough Therapy for Rare Genetic Disorders

Fortuity Pharma

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Lead Collaborator

Dr Bruce Bloom

Dr. Bruce Bloom is a biotech leader and social entrepreneur who continues to work collaboratively to advance effective and affordable treatments for rare disease patients globally.

- **Chief Collaboration Officer at Healx**, a biotech company using AI and drug redevelopment to create therapies for rare diseases
- **CEO of Fortuity Pharma**, a public-benefit corporation focused on developing affordable therapies for rare diseases using existing drugs and nutraceuticals
- **Founder of Cures Within Reach**, a nonprofit that has developed over a dozen therapies for patients and created CureAccelerator®, a drug redevelopment collaboration platform
- **Chief Science Officer** for the Kabuki Syndrome Foundation and Goldman Philanthropic Partnerships, and an **Ashoka Social Entrepreneur Fellow**
- **Chair or member of scientific and patient advisory boards**, including the Vanderbilt Institute for Clinical and Translational Research External Advisory Board, Patient Advisory Board Chair for the Institute for Translational Medicine, Executive Board member of Mission:Cure, Science Advisory Boards of the Dr. Ralph and Marian Falk Medical Research Trust, Beacon for Rare Disease Charity, Westchester Biotech Project and ReBootRx, and the editorial board of ASSAY and Drug Development Technologies.

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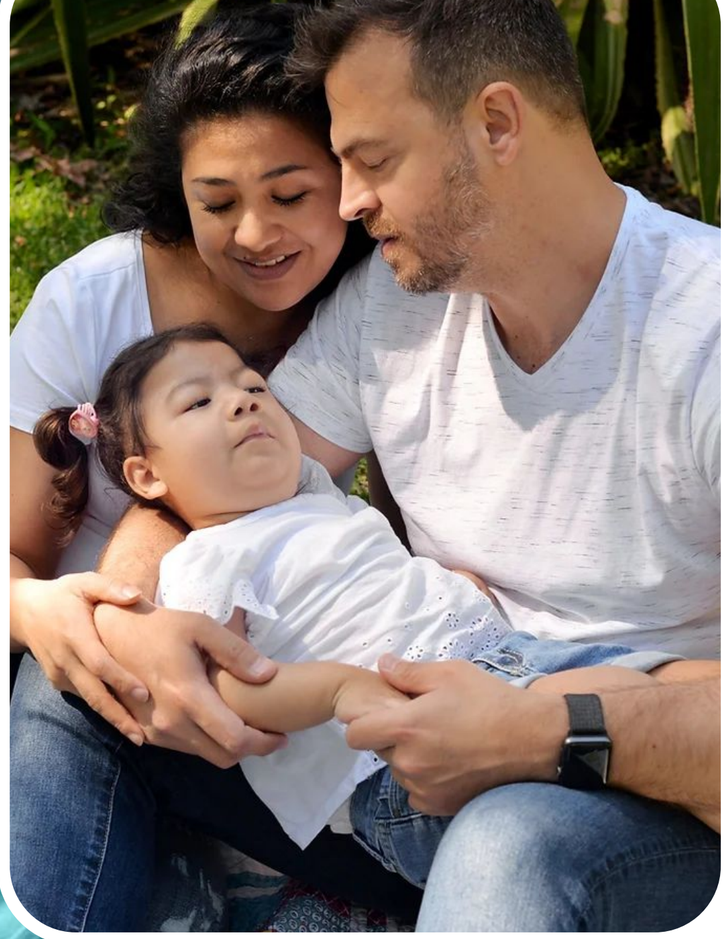

Our inspiration

N=1 trial of amlexanox in WOREE syndrome

- Lucia has WOREE syndrome, an ultra-rare condition caused by recessive mutation of the *WWOX* gene
- Her **nonsense mutation** was identified as a potential treatment target and **treatment with amlexanox led to significant improvements** in Lucia
- Amlexanox was withdrawn from the market in 2019 and while struggling to source more amlexanox, Lucia's condition regressed

FORTUITY PHARMA is a public-benefit corporation that has been established to bring amlexanox back to the market, to potentially benefit Lucia and many more rare disease patients.

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Rarepurposing

Our mission is to bring effective and affordable therapies to the rare disease community by finding new uses for existing drugs and nutraceuticals.

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Amlexanox

An anti-inflammatory drug with established safety profile

- Originally approved for asthma in 1987, it has been used chronically with low side effects for a wide variety of conditions including mouth ulcers and diabetes
- Discontinued in 2019 due to declining commercial demand and market competition

Cheap and easy to manufacture

- Manufacturing is a 3 step process from easy to secure initial substrates

Preclinical testing proves success in multiple rare disease models

- Reads through premature stop codons inmany rare diseases, including cystic fibrosis, Charcot-Marie-Tooth disease, Duchenne muscular dystrophy, Aspartylglucosaminuria, epidermolysis bullosa
- May work better in some genotypes than in others

Potential for 7 year exclusivity

- Possible FDA approval with Orphan Drug Designation
- Some work done on analogues and potential for patent protection through reformulation work

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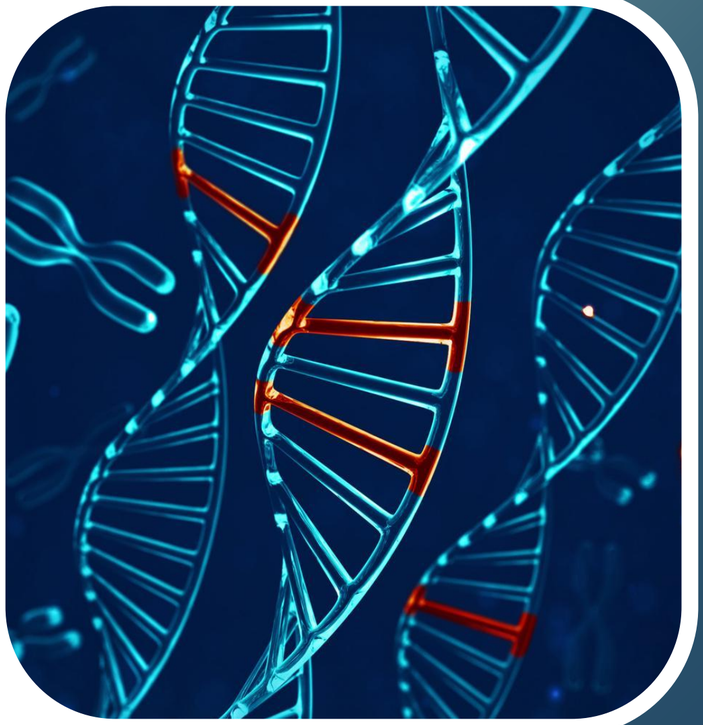
Mechanisms of action

01

Read-through premature stop codon (PTC)

A **nonsense point mutation** can lead to a Premature Stop Codon (PTC), which signals the ribosome to stop translation, resulting in a truncated protein that has little or no function.

Amlexanox **crosses the blood-brain barrier** and has been shown in preclinical models to **promote read-through of the PTC**. It interacts with the ribosomal A-site, mimicking the structure of aminoacyl-tRNA, allowing the ribosome to bypass PTCs to produce full-length, functional proteins.



02

Inhibition of Nonsense Mediated Decay (NMD)

NMD is a cellular process that normally degrades mRNAs with PTCs. Amlexanox interferes with the interaction between NMD factors and the mRNA inhibiting NMD.

This mechanism has been shown to have therapeutic potential in certain genetic disorders and enhance the efficacy of exon skipping therapy. Patients taking amlexanox chronically for asthma did not show any read through or NMD-related side effects.

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Current development plan

01 **GMP manufacturing**

Collaborated with drug manufacturers to produce GMP-grade amlexanox.

02 **Clinical planning**

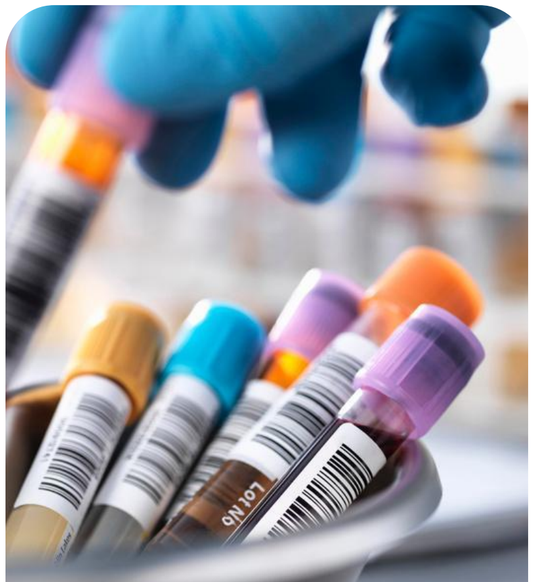
Identifying initial rare conditions that could quickly show benefit from amlexanox and conduct work required for IND-filing (~$50k).

03 **Clinical trial**

Planning an investigator-led **proof of concept trial** at Vanderbilt University in one rare disease, followed by a **basket trial** of in patients with the nonsense genotype in multiple rare diseases.

04 **Patient impact**

Make amlexanox available to patients as quickly as possible at a very reasonable cost through on-label, off-label or compassionate use.



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Our partners so far

BRIGHT PATH™

ON DEMAND PHARMACEUTICALS

Drug manufacturers

Several companies with specific missions to make clinical grade drugs quickly have provided pro bono support to create enough amlexanox to be tested in patient cell lines andto verify the speed and cost of making this drug.

Clara Tang, PhD

Dr. Tang is providing significant operational and scientific support for Fortuity Pharma. She has broad rare disease and start-up experience from her work atr Healx and Kabuki Syndrome Foundation.

WWOX Foundation

WWOX Foundation

Several parents of individual with WOREE syndrome, caused by a defect in the WWOS gene, have experience with amlexanox. One of them provided the drug to their child with significant improvement.

Sitta Sittampalam, PhD

Dr. Sittampalam Is a former Senior Advisor to the Director of the National Center for Advancing Translational Science (NCATS) and a global expert in drug repurposing

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We are looking for a specific subgroup of rare diseases to help validate this potential therapy

01

Autosomal Recessive Rare disease with Loss of Function

For many autosomal recessive conditions, even a modest increase in functional protein levels can be beneficial. Autosomal dominant conditions are more complex, often requiring precise dosage for therapeutic benefit whilst avoiding an overload of it.

02

Genotype of a nonsense mutations leading to PTC

Amlexanox can promote readthrough of premature stop codons, potentially restoring functional protein production.

03

Clear and quick outcome measures

Needed to ensure timely, accurate assessments of treatment efficacy and safety.

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If your rare disease of interest matches these criteria, please get in touch with us to discuss how we might work together!

GET IN TOUCH

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