Designed for Life

Synthetic Biotic Medicines for the Treatment of PKU

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Global PKU Patient Conference
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A new class of medicines

Synthetic Biotic platform

- Non-pathogenic bacterial chassis
- Programmable, engineered

Potential Treatment for PKU

- Consumes toxic metabolites from the GI tract
- Potential treatment for PKU and other allied disorders

Our goal is to develop targeted therapies Synthetic Biotic medicines for the treatment of rare and metabolic disease
A potential new approach to managing phe

Our approach
Oral therapy, 3 x day with meals

Convert dietary Phe to harmless metabolites (TCA)
Reduce plasma Phe

Our aims
Lower blood Phe
Addition of more natural protein into the diet

Synlogic has initiated a Ph2 Study in PKU patients (SynPheny)
How do Synthetic Biotic medicines for PKU work?

**Amino acids from dietary proteins**
(absorption and recirculation)

Healthy

Phenylalanine
Hydroxylase (PAH) converts
Phe into Tyrosine

PKU

Phenylalanine (Phe)

Impaired PAH

Accumulation of Phe to toxic levels

SYNB1618

Manage Phe levels

**Engineered Probiotic Bacteria: E. coli Nissle**
Components of Synthetic Genetic Circuit

Phenylalanine (Phe)

PAL3

Phe

Phe

LAAD

Phenylpyruvate (PP)

Phenyl-lactic Acid (PLA)

Hippuric Acid (HA)

(TCA)

ΔdapA

Trans-cinnamic acid (TCA)
SynPheny-1: Phase 2 Proof of Concept Study Ongoing
Currently Recruiting in the United States

Diet run-in 6 days

Baseline Fasting Phe
Dose 1
1e11
3 days
D5-Phe AUC

Dose 2
3e11
3 days

Dose 3
1e12
7 days

Day 14 Fasting Phe
Dose 4
2e12
2 days
D5-Phe AUC

ClinicalTrials.gov NCT04534842
Study website https://pkuresearchstudy.com/
PKU Patient Survey
Patient Survey: Understanding the Needs of PKU

Goal

Understanding the daily challenges PKU patients face with a focus on Phe levels, dietary management, and need for additional natural protein in their diet

Method

Online survey of PKU patients and parents/caregivers together with NPKUA and CanPKU
Participants

- 64 PKU patients (55% US)
- 77 parents/caregivers (51% US)

- 40.6% of adults and 53.2% of children on Kuvan

- Mean daily natural protein intake was
  - 25.3 g in adults (range 5-78)
  - 19.1 g in children (range 3-90)

- Mean daily Phe intake was
  - 1267 mg in adults (range 250-3900)
  - 953 mg in children (range 150-4500)
Large proportion of PKU patients not at target
2 in 3 adults and 1 in 3 children did not reach target of < 360 µmol/L

<table>
<thead>
<tr>
<th>Phe Level</th>
<th>Adults</th>
<th></th>
<th>Children</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>120 - 360 µmol/L</td>
<td>3.1%</td>
<td>50.6%</td>
<td>3.9%</td>
<td></td>
</tr>
<tr>
<td>360-600 µmol/L</td>
<td>29.7%</td>
<td>23.4%</td>
<td>14.3%</td>
<td></td>
</tr>
<tr>
<td>&gt;600 µmol/L</td>
<td>29.7%</td>
<td>7.8%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>&lt;120 µmol/L</td>
<td>1.6%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>don't know</td>
<td>35.9%</td>
<td>0%</td>
<td>0%</td>
<td></td>
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</tbody>
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Clear unmet need for novel therapies despite existing treatment options
What are the biggest challenges of the PKU diet?

The PKU diet is clearly difficult to prepare and lacking in variety.
Would you like to increase the amount of natural protein in your diet?

A small amount (2-3g) of additional natural protein is considered meaningful.

Patient & Caregiver Response

<table>
<thead>
<tr>
<th></th>
<th>Patient (n=64)</th>
<th>Parent/Caregiver (n=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>92.2%</td>
<td>96.1%</td>
</tr>
<tr>
<td>No</td>
<td>7.8%</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

Examples of foods with 2-3g of protein:

- 1 slice white bread
- 1/2 cup broccoli
- 1/2 cup regular cereal
- 1 medium potato

Protein in Adults

- Total=62
- 2-3g: 53.2%
- 4-5g: 14.5%
- 6-7g: 11.3%
- 8-9g: 12.9%
- 10-15g: 1.6%
- 16-20g: 1.6%

Protein in Children

- Total=77
- 2-3g: 80.5%
- 4-5g: 7.8%
- 6-7g: 6.5%
- 8-9g: 3.9%
- 10-15g: 1.3%
- 16-20g: 1.3%
Key takeaways
Conducted together with National PKU Alliance and Canadian PKU and Allied Disorders

A significant proportion of both adult and pediatric PKU patients are not well controlled (Phe levels >360 umol/L)

Virtually all PKU Patients (or their caregivers) want to increase the amount of natural protein in their diet

Even 2-3 g of additional natural protein per day would be considered meaningful by the majority of PKU patients (or their caregivers)
Thank You!

Find us on ClinicalTrials.gov
ct.gov #: NCT04534842

Visit our study website
https://pkuresearchstudy.com/

Contact us at
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