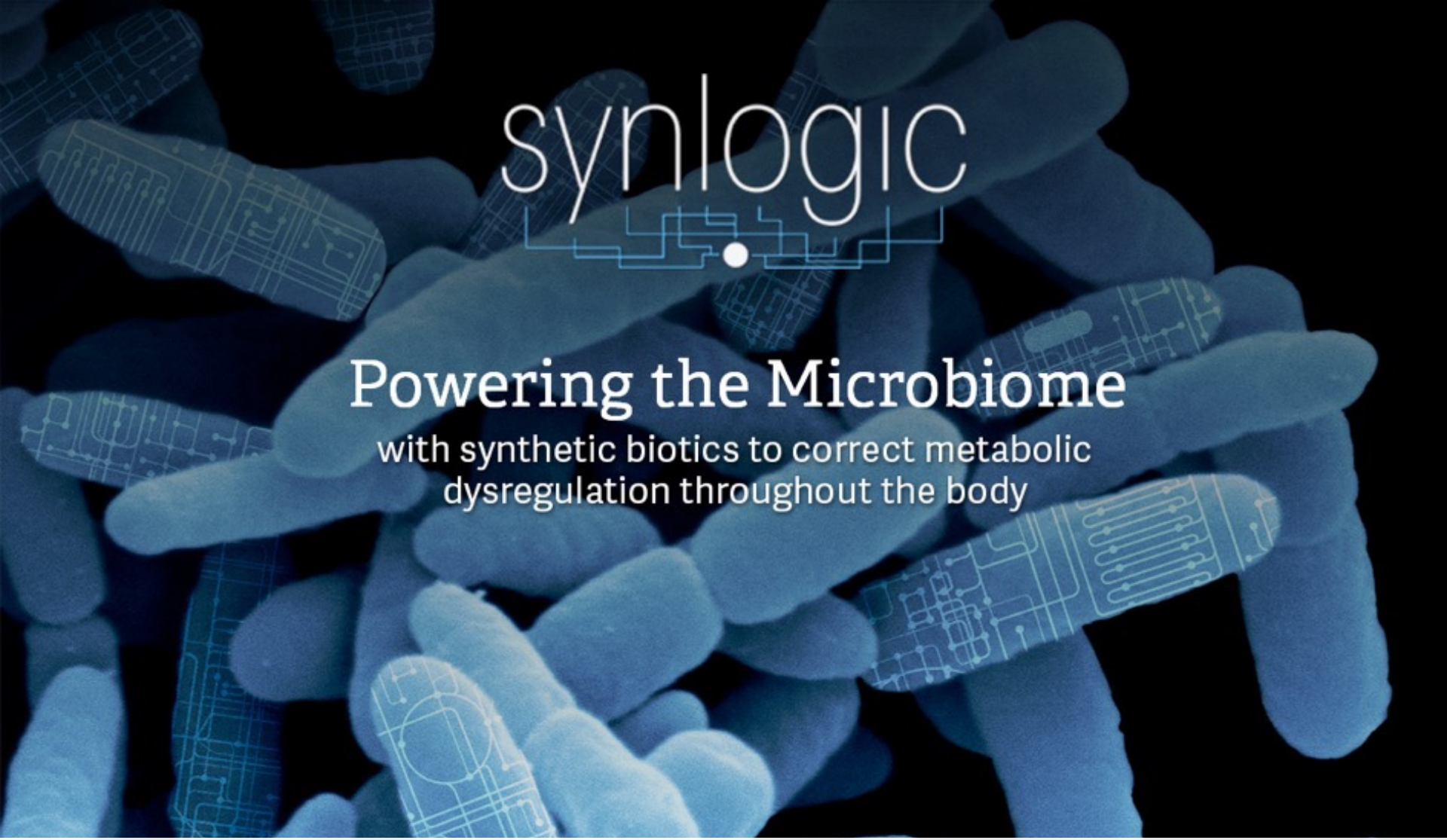


Corporate & PKU Overview

February 2016

Corporate History

2017 UCD & PKU Programs: Ph1b Data

[YE2016/1H2017]
IND Filing

2016

December 2015:
$40M Series B round TS signed

July 2015:
IBD collaboration signed with AbbVie

2015

November 2014:
Start of lab operations

July/October 2014:
$29.4M Series A round: Atlas Ventures, NEA, and B&M Gates Foundation)

2014

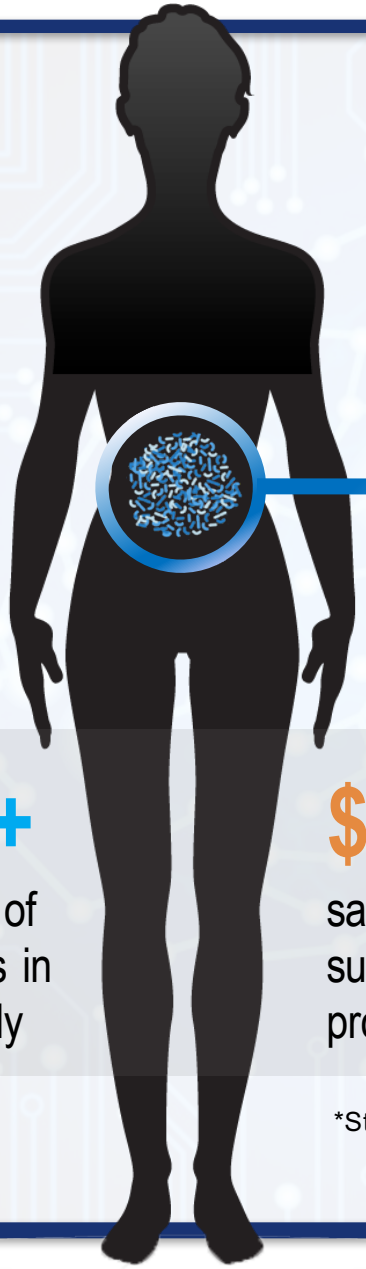
Scientific Co-Founders: Dr. James Collins & Dr. Timothy Lu

March 2013:
Synlogic Incorporated (fka TMC Therapeutics; seeded at Atlas Venture)

2013

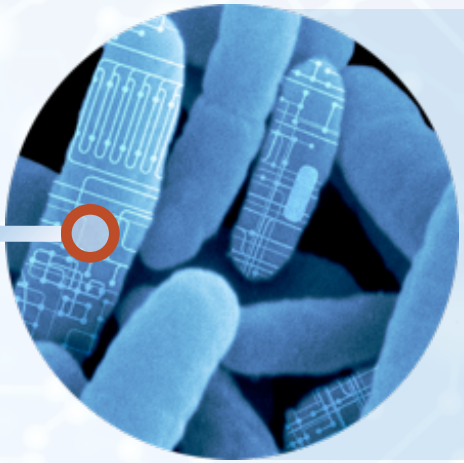
2

SYNTHETIC BIOTICS: Precision Programmed Probiotics to Treat Serious Diseases



Precision Programming

Synthetic Biotics



- **Selective and predictable** pharmacology
- Designed to be **safe**
- **Oral** administration
- Designed to **perform metabolic functions in the gut** to treat diseases

400+
species of probiotics in our body

$3.5 B
sales probiotic supplements & products, U.S.* (2015)

*Statista 2016

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Synthetic Biotics: A New Class of Drugs

Synthetic

- **Engineered** bacteria
- Genetic circuits that perform **metabolic transformations**
- Designed synthetically to **degrade metabolites** that induce disease or **synthesize substances** that can treat disease

Biotics

- **Probiotic bacteria:** *E. coli* Nissle
- Derived from **natural human microbiome**
- **Extensive safety in humans** as probiotic
- Daily, **oral administration**

Synthetic Biotics

Therapeutic action from the microbiome to correct metabolic dysregulation throughout the body

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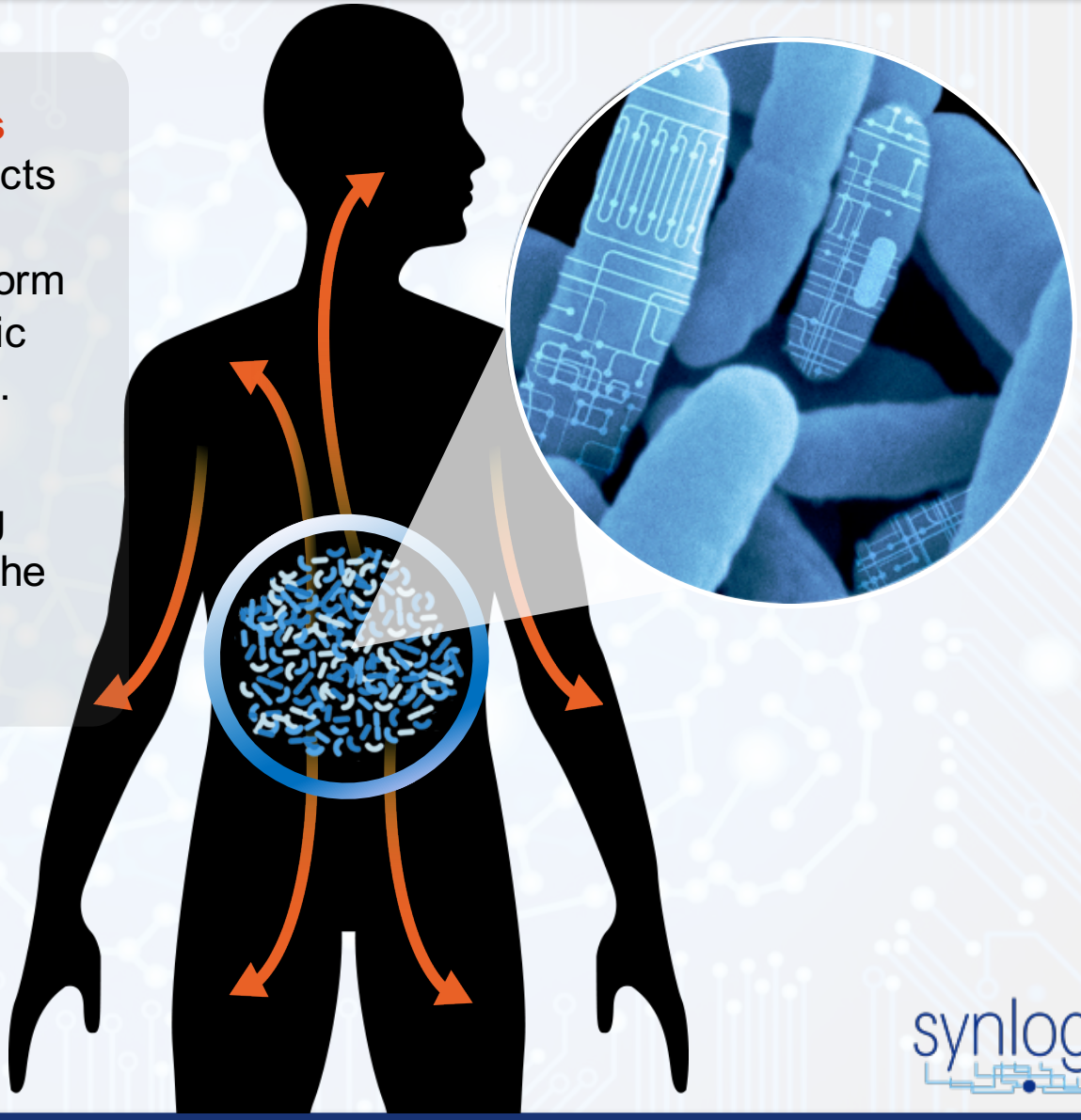
Synthetic Biotics: Therapeutics that Operate from our Natural Microbiome

Synlogic's **synthetic biotics** are oral bacterial drug products that blend with the patient microbiome where they perform their programmed therapeutic metabolic transformations …

…. to correct metabolite dysregulation that is causing chronic disease throughout the body



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Synlogic is at the Convergence of Two Revolutionary Fields in Life Sciences

2 Revolutionary Fields

Synthetic Biology

Microbiome

Probiotic

Synthetic Biotics

- Transformative therapies
- Pipeline of products
- Value Creation in compressed timeline

Rare Diseases

Major Diseases

Therapeutic Drug Products

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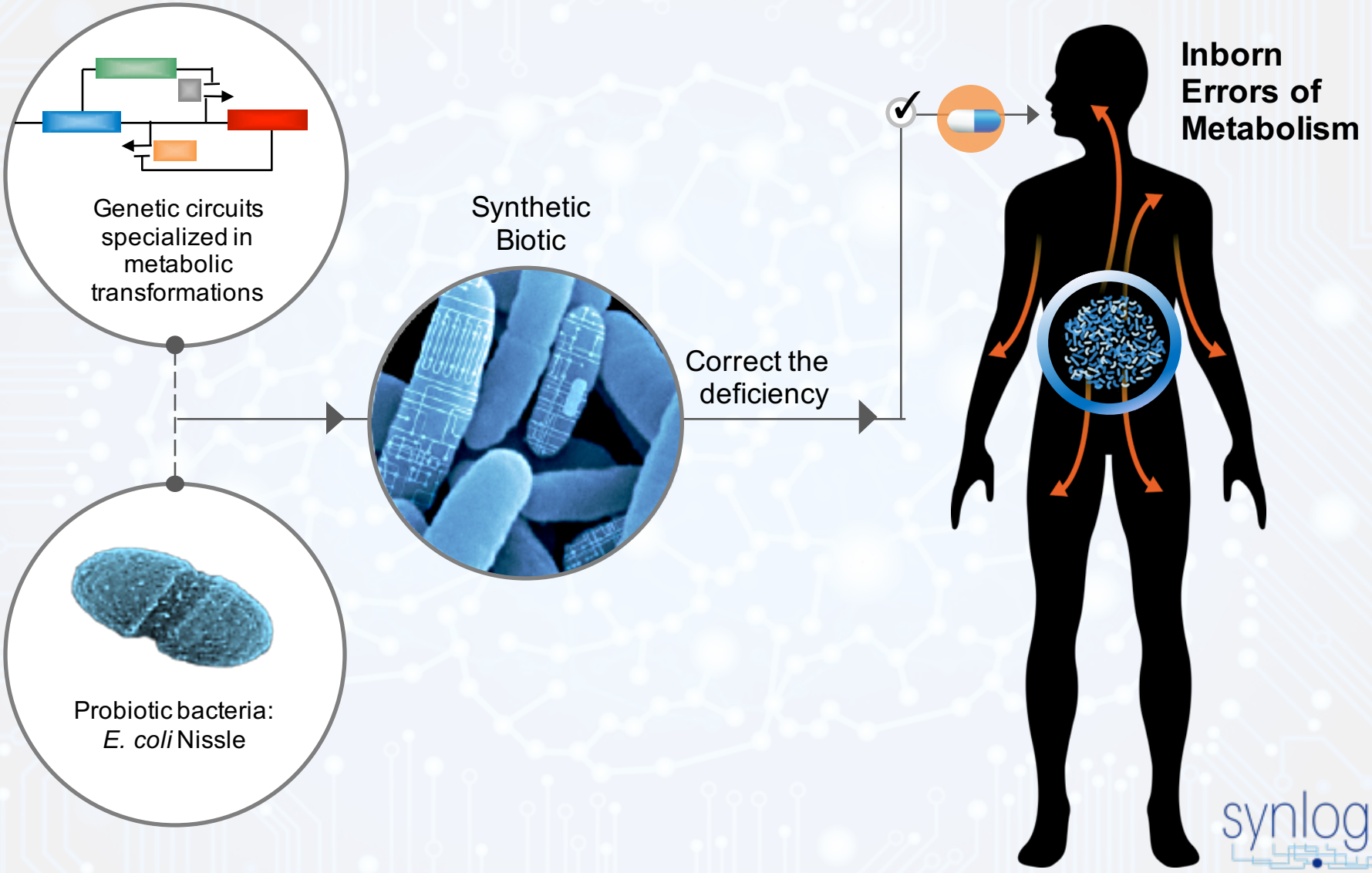
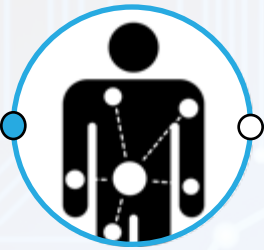
Synlogic's Drug Discovery and Development Approach

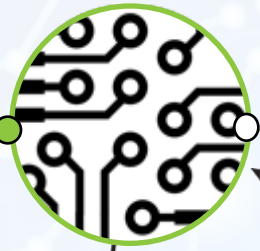


A Simple, Robust and Rapid Platform for Generating Synthetic Biotics



DEFINE

DISEASE PATHWAY

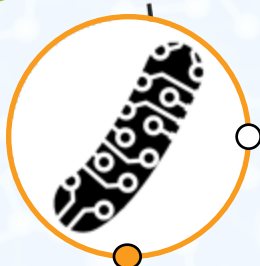


DESIGN

CIRCUIT

ASSIMILATE

IN THE MICROBIOME



BUILD

SYNTHETIC BIOTIC

- Metabolic pathway expertise
- Drug development experience
- Understanding of disease processes
- Differentiated TPP

- Genetic circuits
- Switches
- Bacterial technologies
- Enzyme selection
- Genomic integration technologies

- Bacterial engineering
- "Chassis" optimization
- Bacterial genome integration landing pads
- Stable integration

- System check
- GI dynamics
- Potency in vitro and in vivo
- Blend into microbiome without colonization

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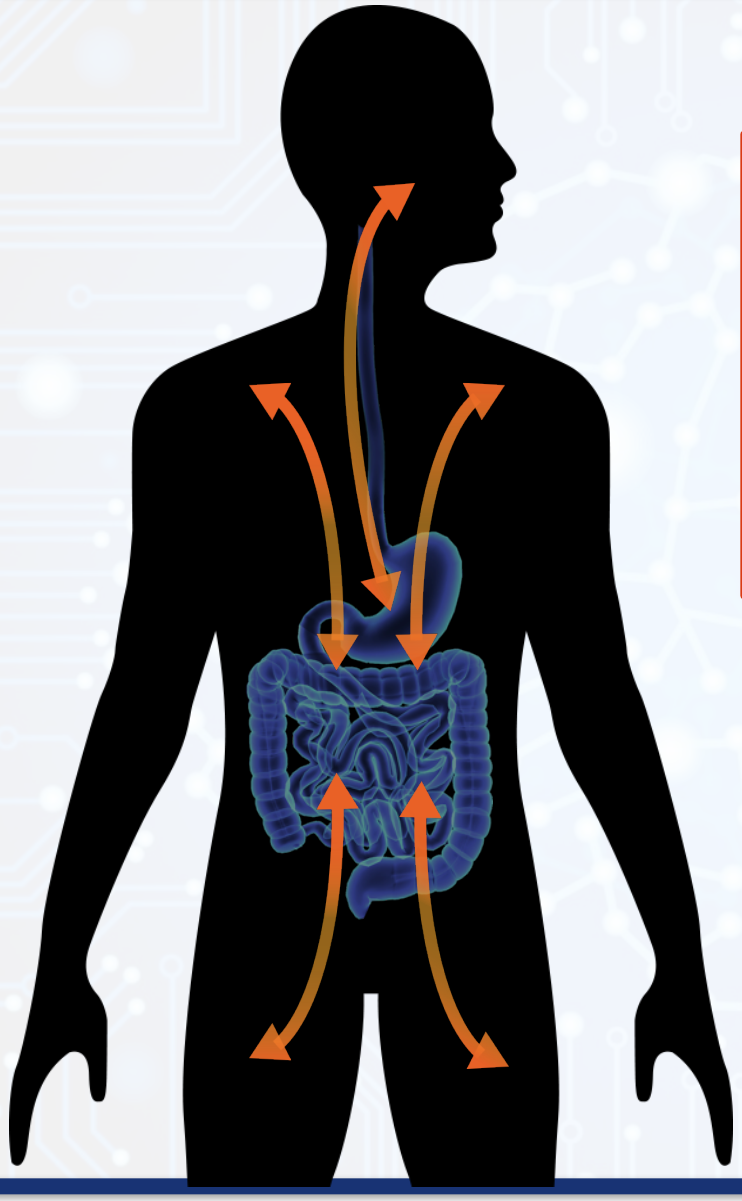
Synlogic's Initial Focus: Inborn Errors of Metabolism



Disease	Toxic Metabolite
Urea Cycle Disorders	Ammonia
Phenylketonuria	Phenylalanine
Organic Acidemias	Propionate
Maple Syrup Urine Disease	Ile, Leu, Val
Homocysteinuria	Homocysteine, Methionine
Xanthinuria Type 1	Xanthine
Primary Hyperoxaluria	Oxalate

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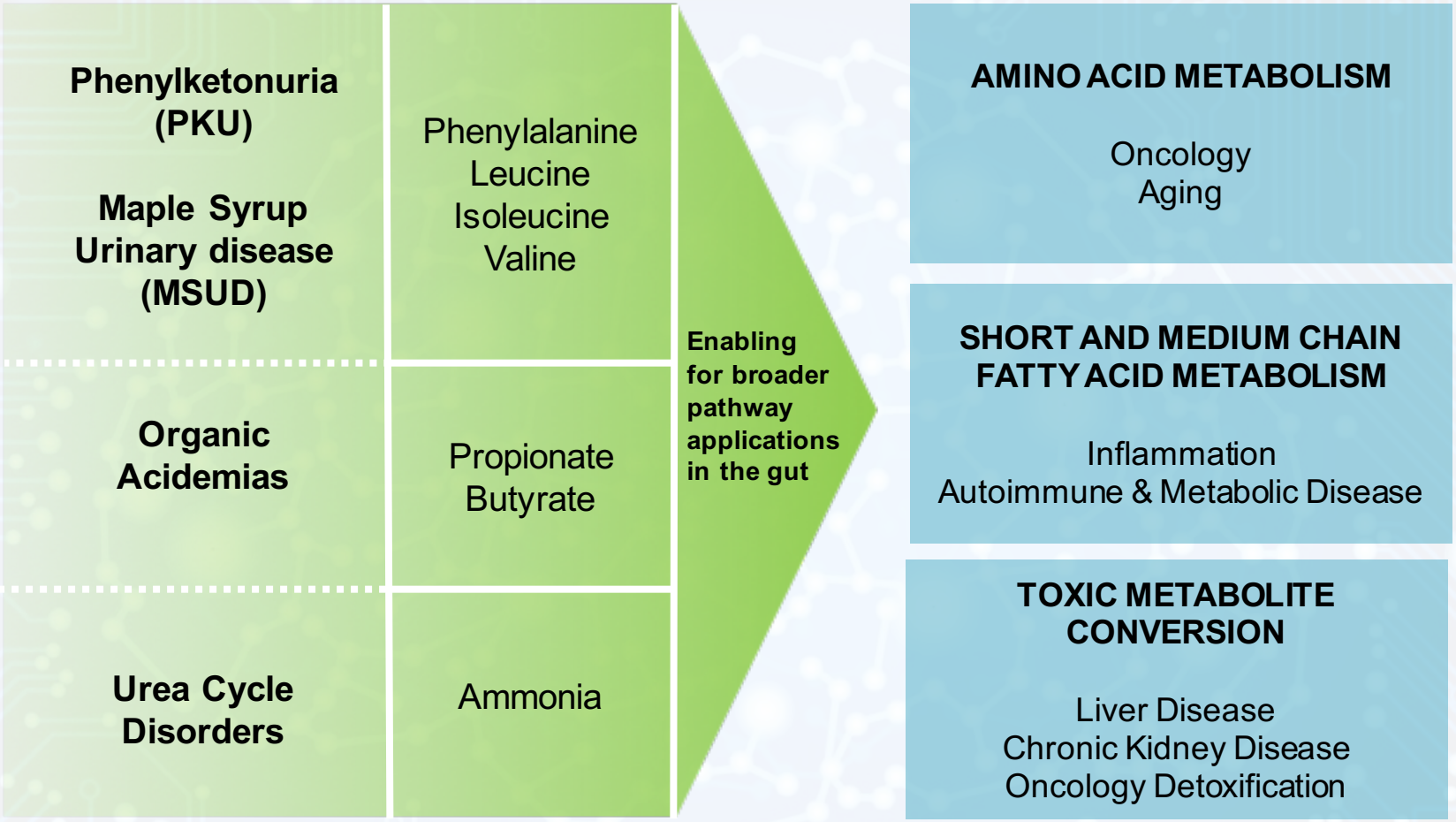
Synthetic Biotics Can Mediate Broad-Range of Metabolite Transformations in the Gut



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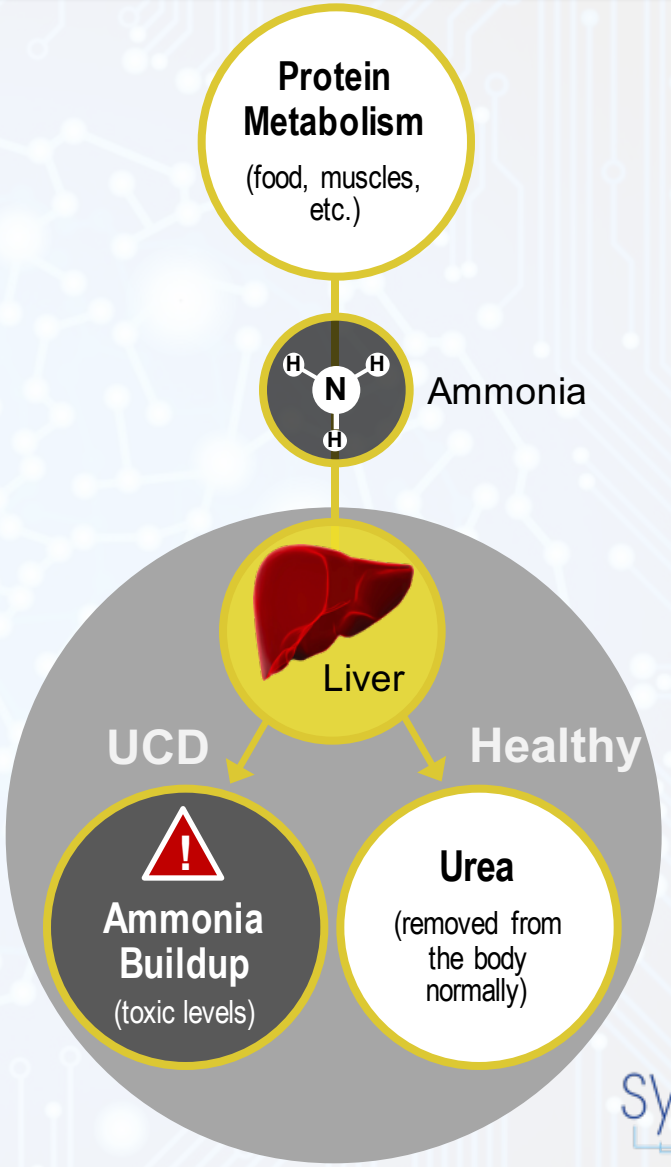
Lead Program I: Urea Cycle Disorders (UCD)

Urea cycle disorders: 2,000-6,000 patients with hereditary disorder (US)

- Genetic defects in Urea Cycle
- Symptoms: vomiting, encephalopathy, respiratory stress, irreversible brain damage, coma and/or death
- Standard of care inadequate– best option is liver transplant

Additional benefit possible for >900,000 hepatic encephalopathy/cirrhosis patients

- Fulminant liver failure, chronic liver failure, cirrhosis, etc.



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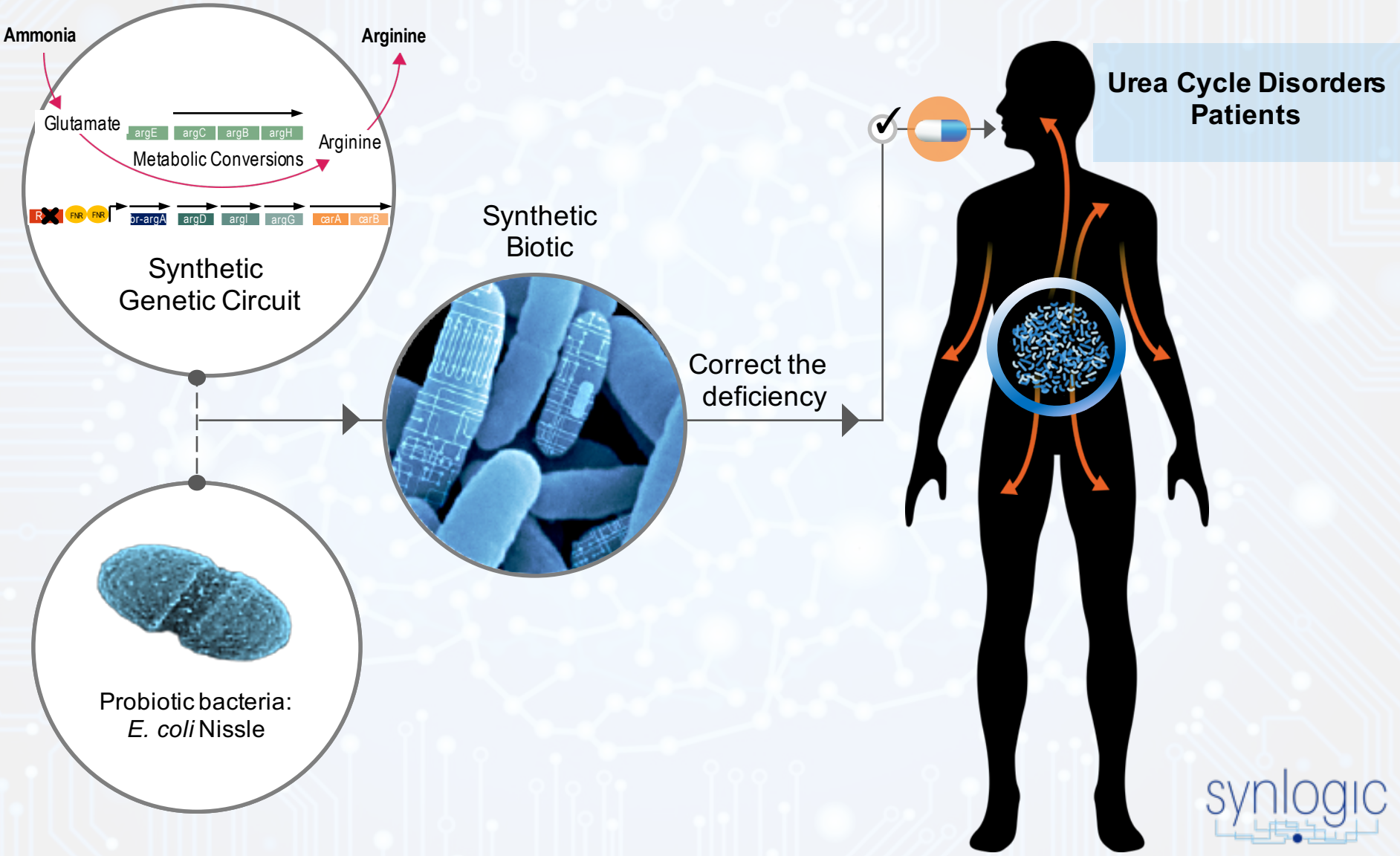
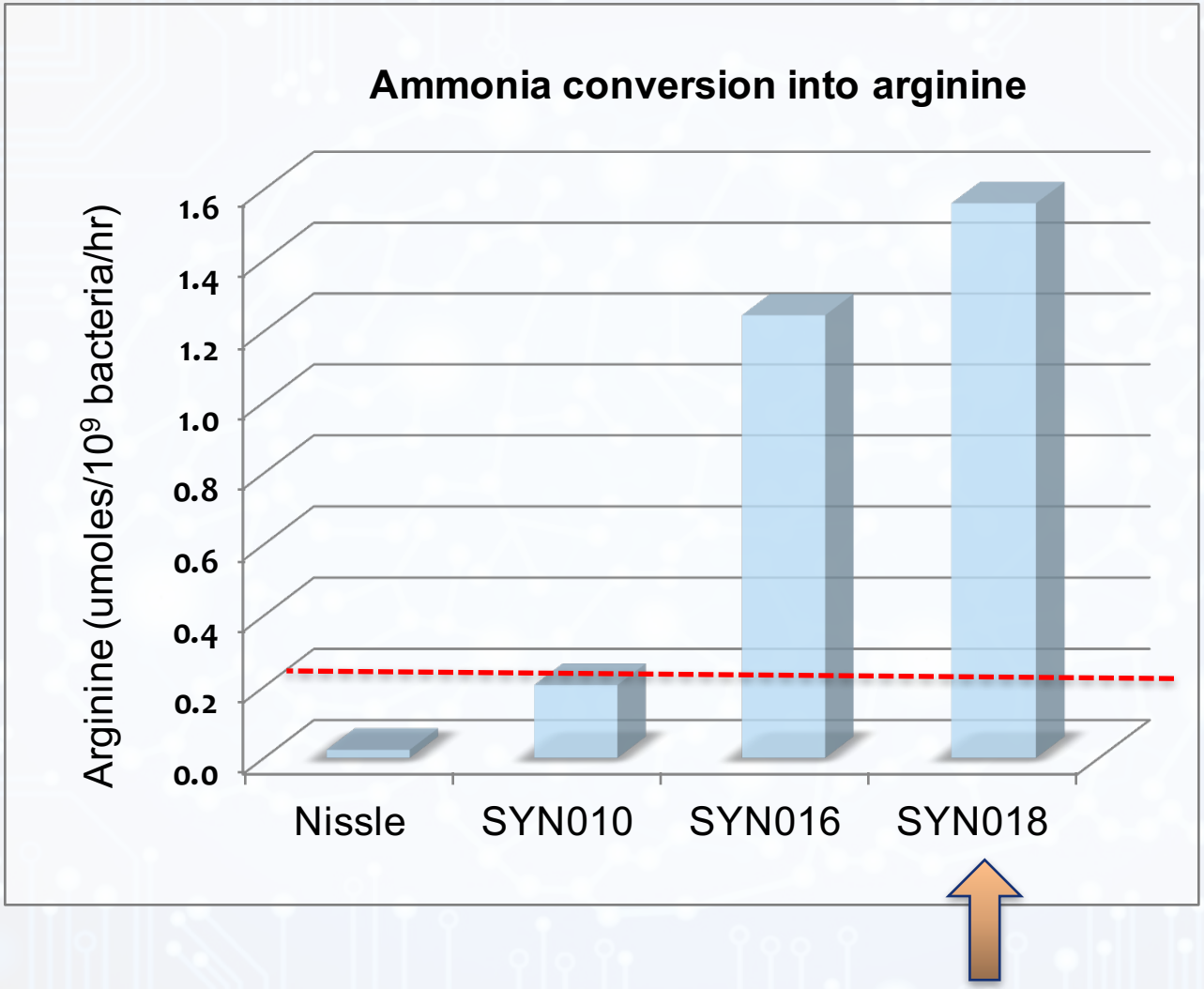
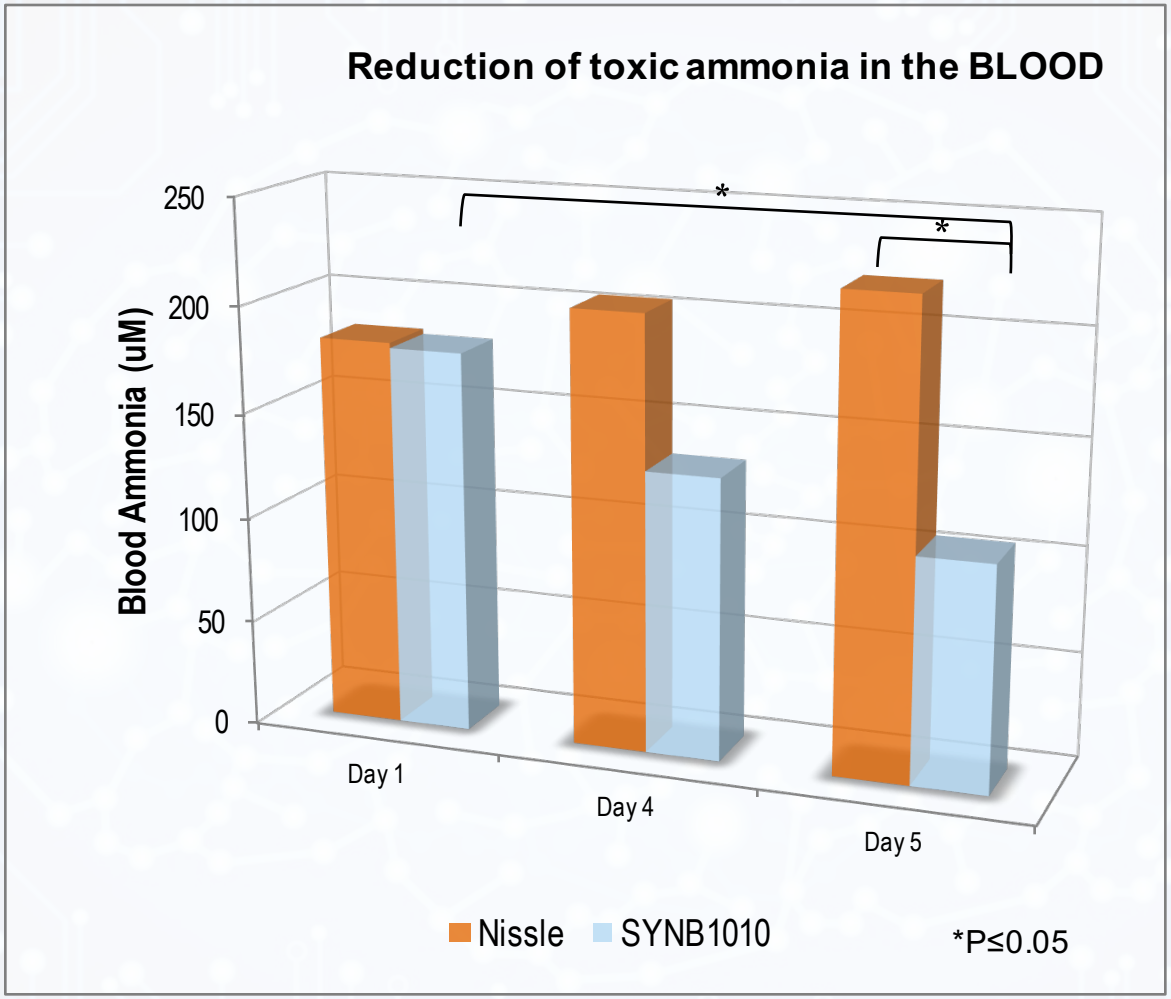
SYNB1010: Conversion of Toxic Ammonia into Beneficial Arginine for the Treatment of UCD



Clinical Candidate Selection: Efficient Ammonia Conversion *In Vitro*



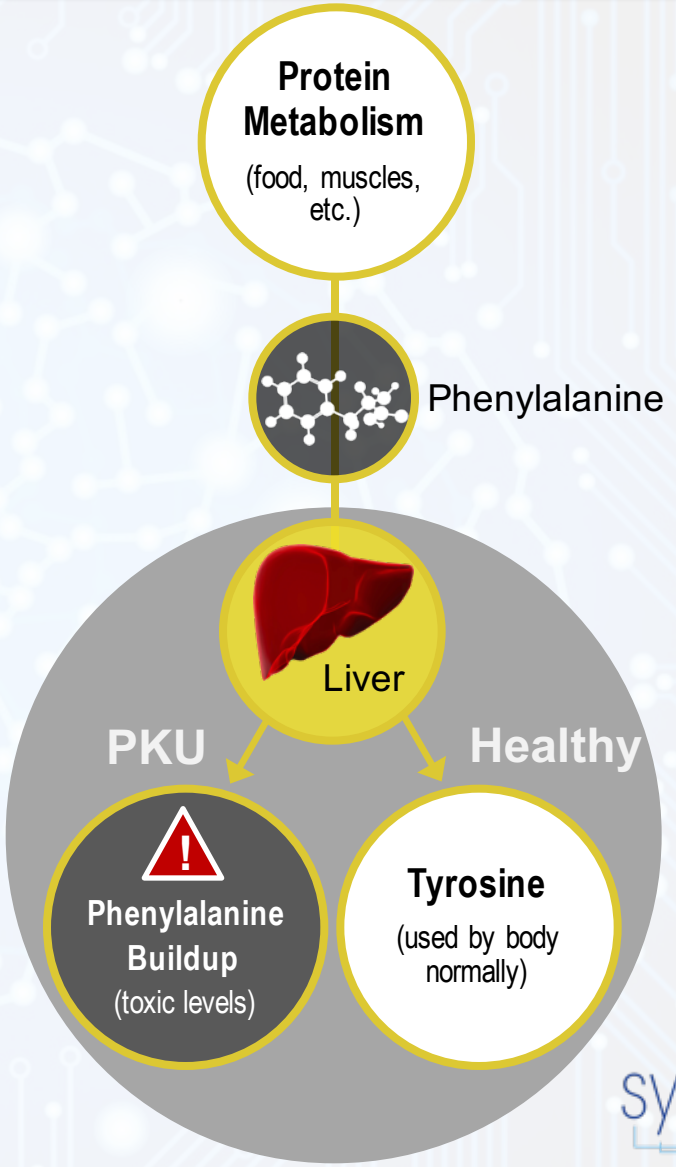
SYNB1010: Efficient Ammonia Conversion *In Vivo* – *Acute* Hepatic Encephalopathy Model



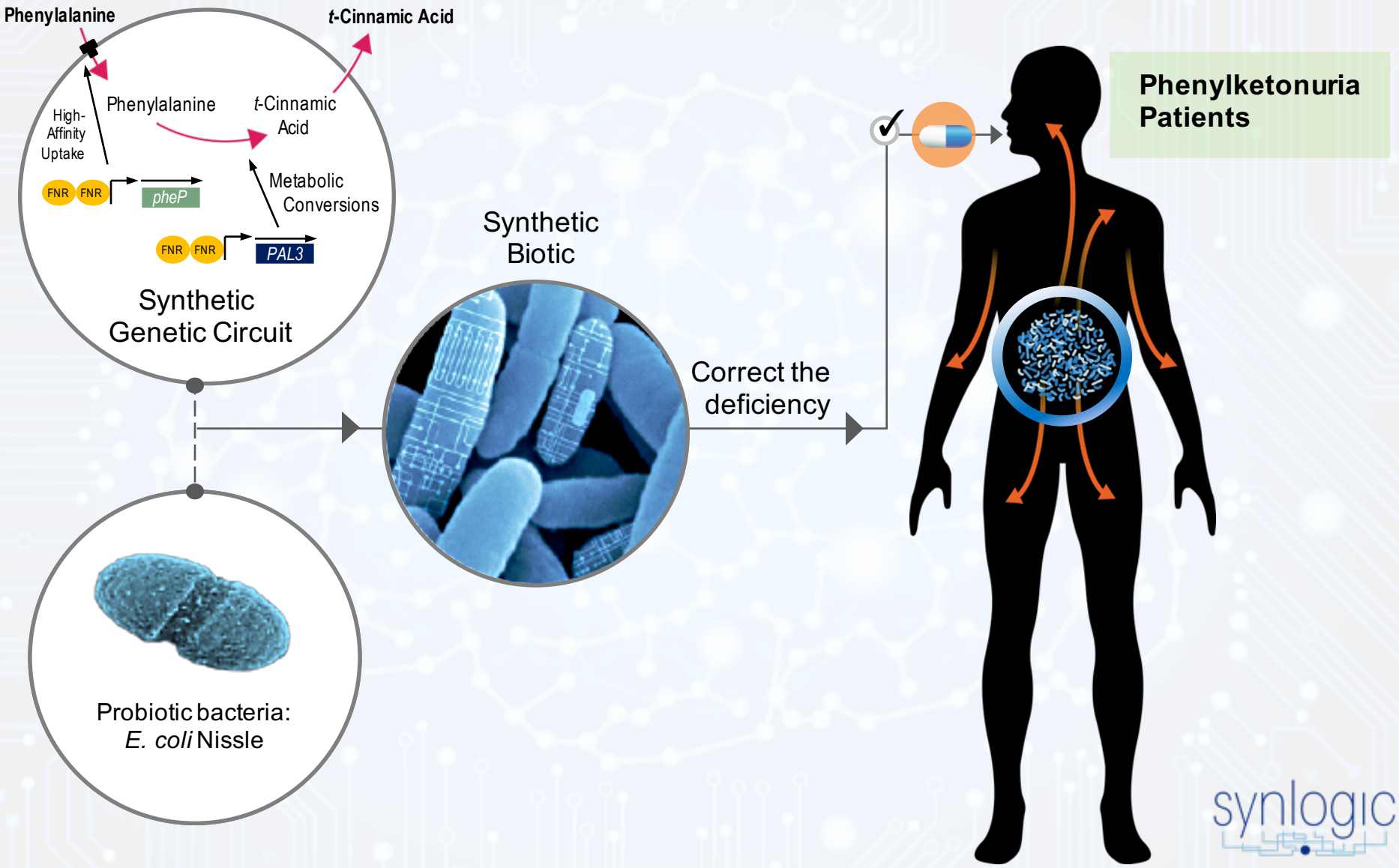
Lead Program II: Phenylketonuria (PKU)

PKU disorders: ~13,000 patients with hereditary disorder (US)

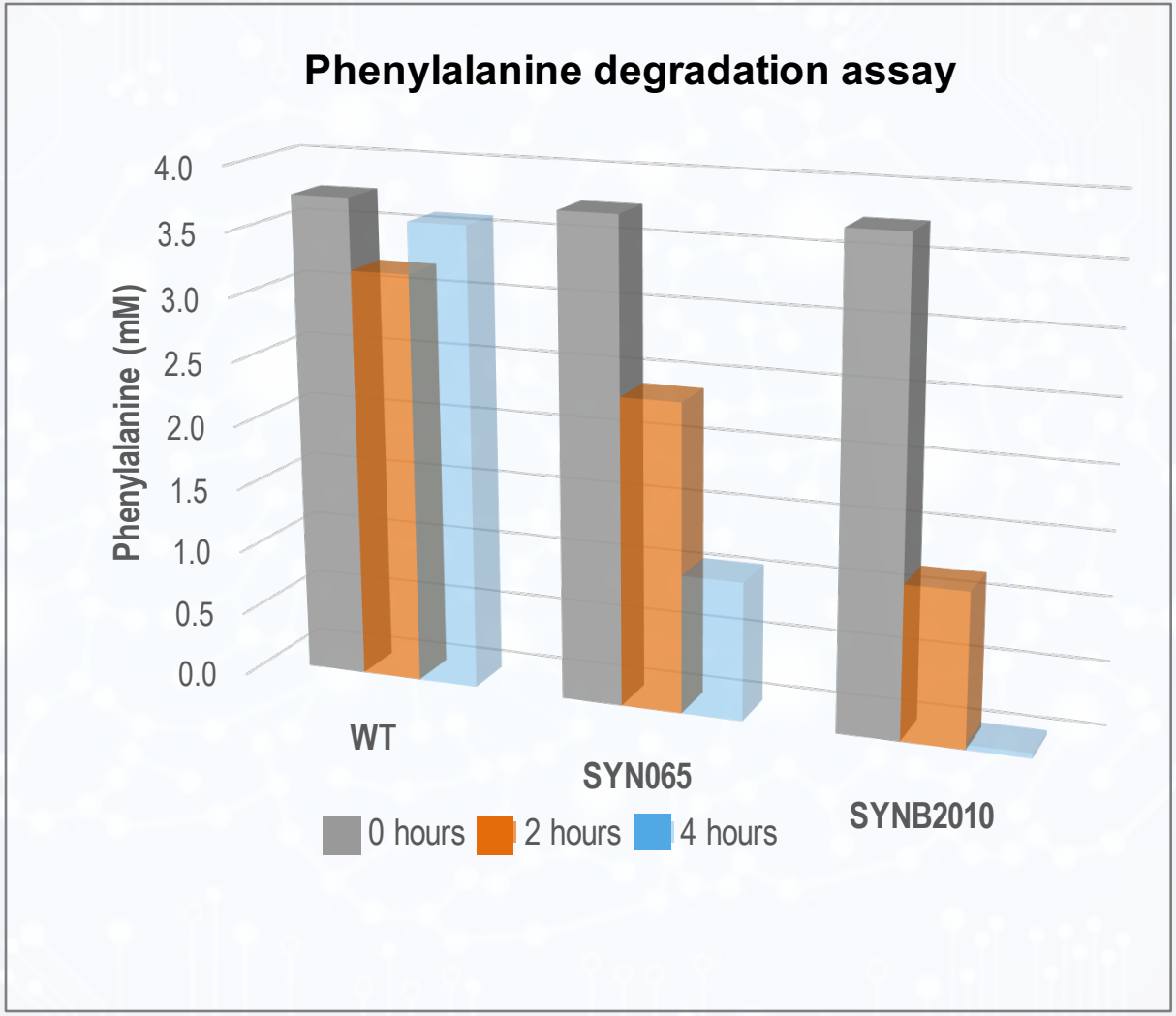
- Genetic defect in phenylalanine hydrolase (PAH) enzyme
- **Symptoms:** mental retardation, convulsions, behavior problems, skin rash, musty body odor
- Standard of care inadequate
- Kids maintained on very low protein diet (NO meat, dairy, dry beans, nuts, eggs)



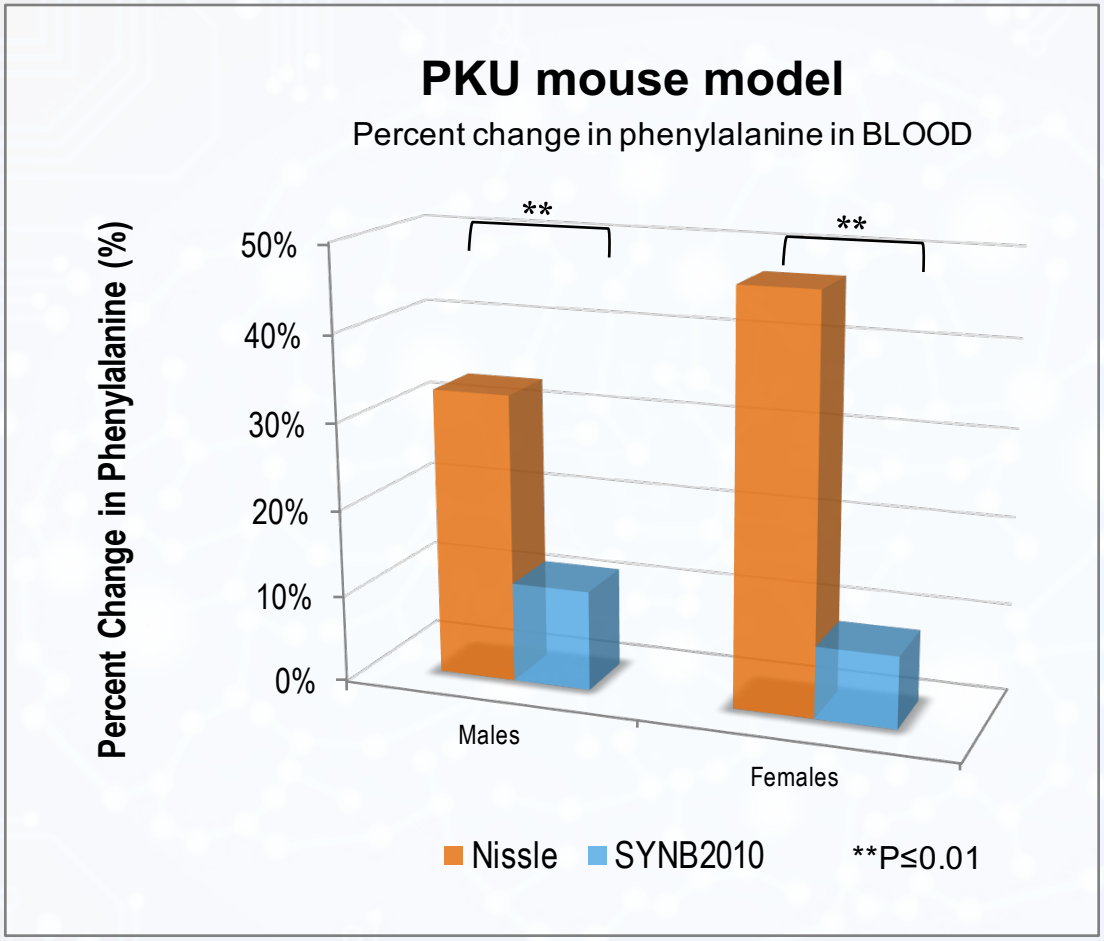
SYNB2010: Degradation of Toxic Phenylalanine for the Treatment of PKU



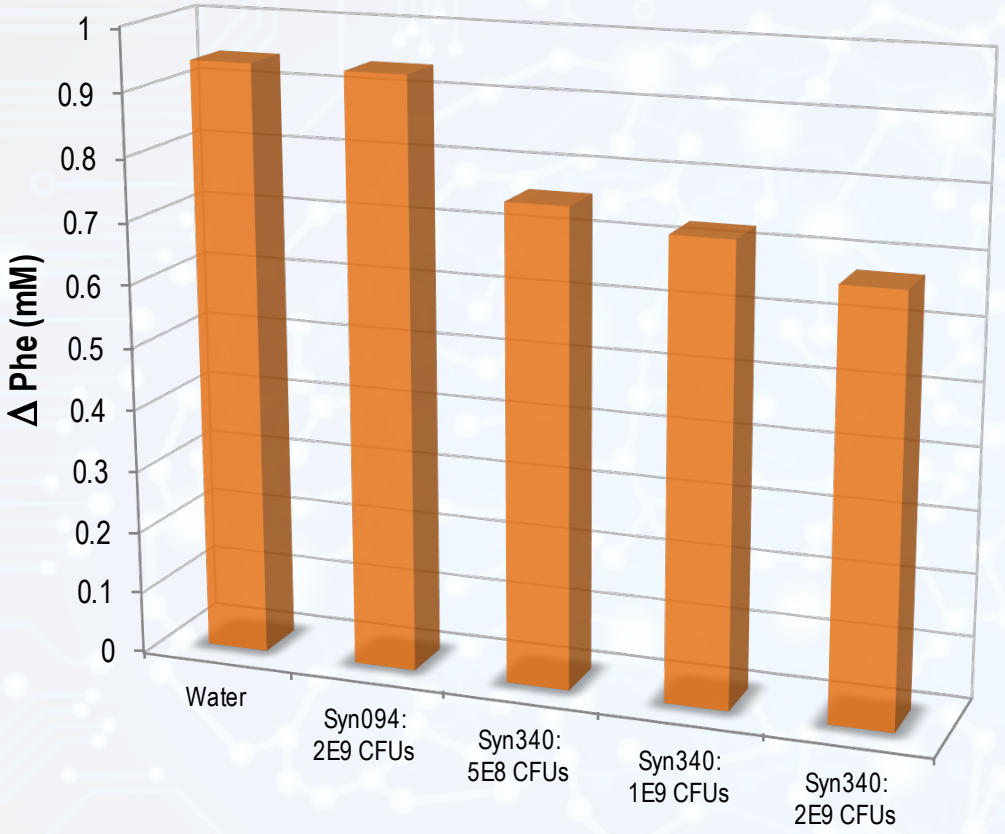
Clinical Candidate SYNB2010: Efficient Phenylalanine Degradation *In Vitro*



Clinical Candidate SYNB2010: Efficient Phenylalanine Degradation *In Vivo*



Dose-Dependent Decrease in Systemic Phe Levels by an FNR-inducible PKU Strain



- Mice were administered Phe subcutaneously (0.1mg/g)
- Following Phe treatment, mice were gavaged at 30 and 90 minutes with SYN94 (parental Nissle strain) or SYN340 (Nissle strain carrying loq copy, FNR-inducible PAL3 gene as well as an FNR-inducible chromosomal insertion of *pheP*)
- Mice were bled at time 0 and at 4 hours post-injection
- SYN340 was able to intercept entero-recirculating Phe and thus blunt the increase in blood Phe observed post Phe injection

Experiment is one representative of 8 studies of this design which consistently show a significant effect of SYN340

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EDC: PK/PD Profiling of SYN2010

Parameter	Value
Maximum burden of Phe in blood of phenylketonuric patient	5000 µmols total Phe Total blood Phe levels: ~1000 µM; 5 L blood (adult)
Phenylalanine consumption target: Phe burden	5000 µmol/day
Target phenylalanine consumption rate: Phe burden	5000 µmol/day/10^{11} bacteria
Lab assay target: Phe burden	2.08 µmol/hr/10^{9} bacteria
Current phenylalanine consumption rate	**4-15 µmol/hr/10^{9} bacteria***
Maximum dietary intake of phenylalanine; in healthy individuals>PKU patients	18000 µmols/day
Phenylalanine consumption target: Phe intake	750 µmols/hr
Target phenylalanine consumption rate: Phe intake	250 µmols/hr/10^{11} X 3 doses
Lab assay target: Phe intake	2.50 µmol/hr/10^{9} bacteria

Note: food intake based on recommended adult consumption of 75 g/day.
PKU pts are primarily children with restricted protein intake.

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Commercial PKU Target Product Profile

BOLD: early development milestones

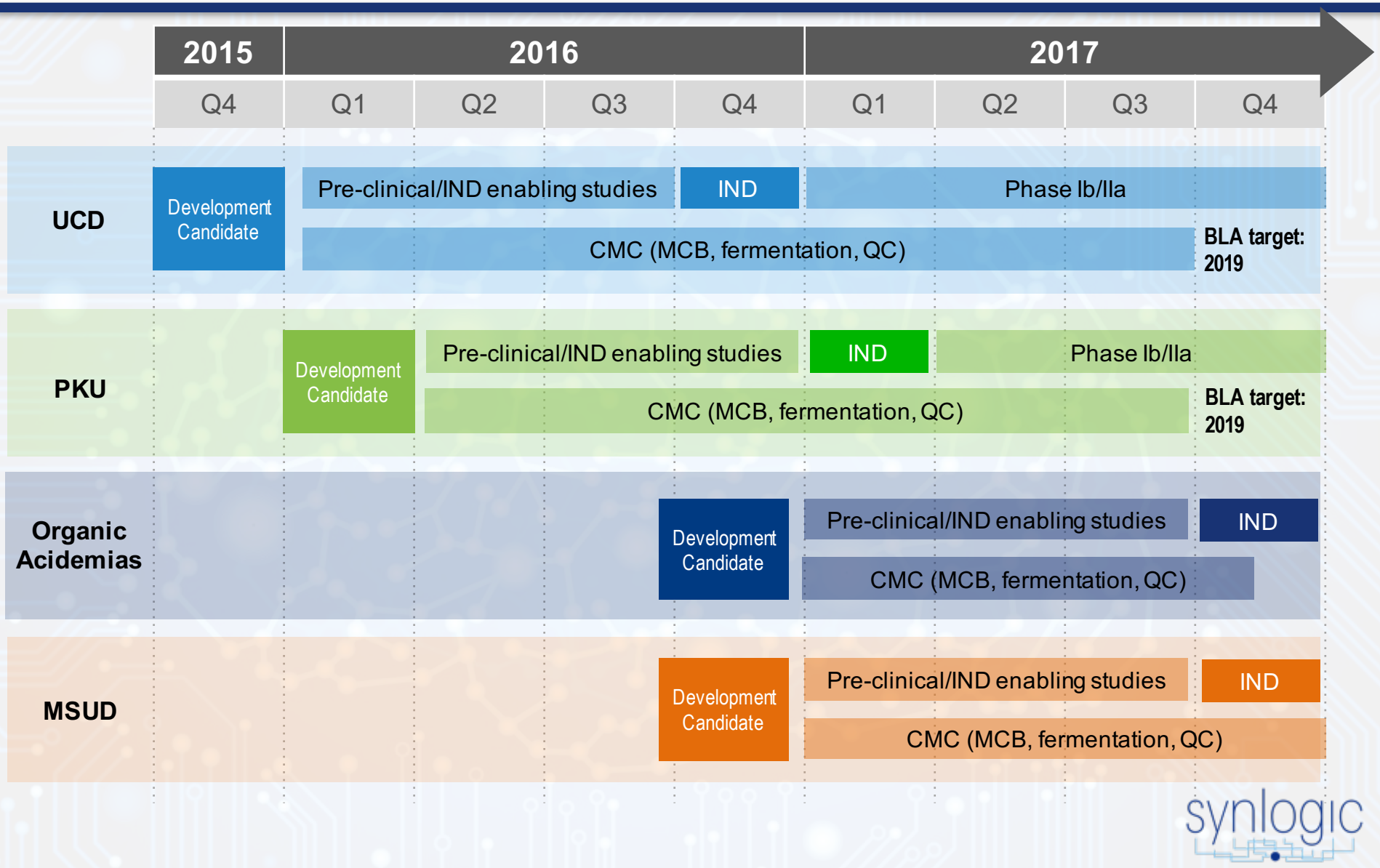
	Attribute	Sapropterin (Approved; Kuvan™)	PEG-PAL (Phase 3)	SYNB2010 (BASE CASE TARGET)	SYNB2010 (BEST CASE TARGET)
Drug	• Indication • **Route of admin.** • **Dose range** • **Dose frequency** • **Duration of treatment**	➢ Hyperphenylalaninemia (BH4 responders only) ➢ Oral with food ➢ 10-20 mg/kg/day ➢ Once daily ➢ Chronic; no immunogenicity	➢ Hyperphenylalaninemia (likely all genetics) ➢ Injectable (self) ➢ 20-40 mg/kg/day ➢ Once daily ➢ Unknown; likely high rate of immunogenicity[1]	➢ Hyperphenylalaninemia (no restrictions on genetics) ➢ **Oral with food** ➢ **1E9-1E11 bacteria** ➢ **Three times daily** ➢ **Chronic**; <10% immunogenicity	➢ Hyperphenylalaninemia (no restrictions on genetics) ➢ Oral without food ➢ 1E7-1E9 bacteria ➢ Once daily ➢ Chronic; no immunogenicity
Clinical	• Population • **Responders** • Restrictions • **Primary endpnt** • Secondary endpnt • Tertiary endpnt • **Adverse reactions** • Contraindications • Monitoring	➢ >1 month of age ➢ <20%; limited mild/mod PKU ➢ Adjunctive to Phe-free diet ➢ ~29% reduction blood Phe[2] ➢ Phe-free diet required ➢ N/A ➢ <15% Grade 1 ➢ None ➢ Monthly blood Phe levels	➢ Adults ➢ 75-90%[1] ➢ Adj. to Phe-free diet ➢ ~54% reduction blood Phe[1] ➢ Phe-free diet required ➢ Executive function/mood ➢ ~80% Grade 1 or higher[1] ➢ Unknown ➢ Frequent blood Phe levels	➢ >4 years of age ➢ **>50% (all genetics & severity)** ➢ Adjunctive to Phe-free diet ➢ **>30% reduction blood Phe** ➢ >20 g/d protein per day ➢ Cognitive/mood improvement ➢ **<20% Grade 1** ➢ None ➢ Monthly blood Phe levels	➢ >1 month of age ➢ >90% of all PKU patients ➢ None; normal diet ➢ >60% reduction blood Phe ➢ >70 g/d protein per day ➢ Cognitive/mood normal ➢ <5% Grade 1 ➢ None ➢ >3 mo Phe monit. intervals

Source: KOL discussions; company websites; Synlogic analyses; publications

[1]Longo, Nicola, et al. "Single-dose, subcutaneous recombinant phenylalanine ammonia lyase conjugated with polyethylene glycol in adult patients with phenylketonuria: an open-label, multicentre, phase 1 dose-escalation trial." *The Lancet* 384.9937 (2014): 37-44.

[2]Levy, Harvey L., et al. "Efficacy of sapropterin dihydrochloride (tetrahydrobiopterin, 6R-BH4) for reduction of phenylalanine concentration in patients with phenylketonuria: a phase III randomised placebo-controlled study." *The Lancet* 370.9586 (2007): 504-510.

Two INDs in Next 4Qs: Four Clinical Programs in 2017



Synthetic Biotics Designed to be Safe: Regulatory Strategy

Inherent Safety

- Nissle -background chassis is a naturally occurring probiotic widely used
- Isolated from human microbiome
- Extensive human safety profile
- Genes being refactored are derived from human genome or commensal microorganism
- Transient: non-colonizing probiotic well characterized

Synlogic Strategy:

- Phase 0 Nissle study
- NHP Nissle study
- Nissle bioinformatics for pathogenic genes and prevalence
- Synthetic circuit gene etiology
- Literature curation
- Viability characterization for Synthetic Biotic
  - Time course analysis in vitro
  - Shedding/clearance in vivo
  - Auxotroph challenge (DapA, thyA, etc. single/dual)

Regulatory Standards for Monitoring

- Industry leaders in setting biocontainment criteria
- Highest standard for biocontainment
- Engineered microorganism
- Probiotic
- Focus on level vs mechanism
- Auxotrophy
- Kill Switch

Synlogic Strategy:

- Monitoring Approaches:
  - Single/dual auxotrophy: synthetic amino acid, gene deletions, inducible auxotrophy
  - Gene-guard plasmids
  - Kill switch: Recombinase-controlled nuclease (toxin/anti-toxin), enhanced sensitivity to antibiotic

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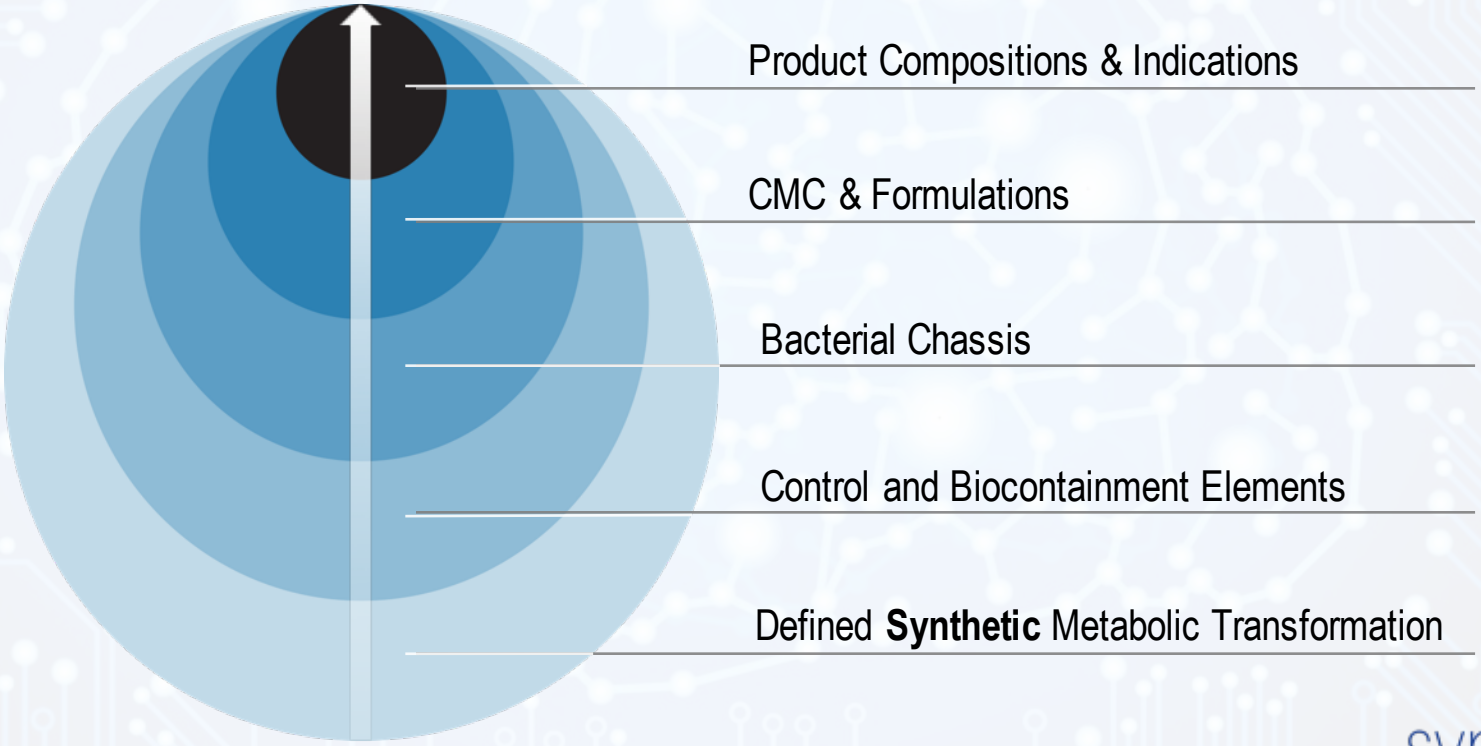
Leading IP Portfolio: Program-Specific IP Provides Comprehensive and Layered Coverage

Formidable Barrier to Entry



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Key Synlogic Takeaways

Novel Therapeutic Class

- **Synthetic Biotics:** Leading the convergence of probiotics and synthetic biology to create novel medicines
- Simple, robust and rapid process for the creation of drug candidates

Robust Pipeline with Orphan Drug Programs

- **At least Two INDs planned in next 4Qs:** UCD and PKU
- **Four clinical programs expected in 2017**

Partnership with AbbVie

- Inflammatory Bowel Disease (IBD)

Dominant Synthetic Biotics IP Portfolio

- 7 Issued/Allowed Patents
- 34 Patent Families
- 100 Pending Patent Applications

Strong Balance Sheet

- Series A: ~$30MM
- Series B: ~$40MM (closing expected in January 2016)
- Seasoned biotech investors: Atlas Venture, NEA, Bill & Melinda Gates Foundation

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Investors & Core Advisors

Investors	SynBio Leaders	Therapeutic Experts
Atlas Venture Peter Barrett Ankit Mahadevia	**Jim Collins** - Scientific co-founder Termeer Professor of Medical Engineering & Science, MIT, Broad Institute, Wyss Institute	**Cammie Lesser** Associate Professor of Medicine, MGH
NEA Ed Mathers	**Tim Lu** - Scientific co-founder Associate Professor of Biological Engineering, MIT	**Wendy Garrett** Associate Professor, Harvard School of Public Health, Broad Institute
The Gates Foundation Charlotte Hubbert	**Kristala Prather** Associate Professor, MIT	**Bill Sandborn** Chief, Division of Gastroenterology, Professor of Medicine, UCSD
	Chris Voigt MIT, Broad Foundry	**Brian Feagan** Professor of Medicine, Robarts Research Institute, University of Western Ontario

Synlogic Management Team

Core team has deep domain & early stage company-building experience

- **CEO:** JC Gutierrez Ramos (Pfizer, GSK, Millennium, Harvard)

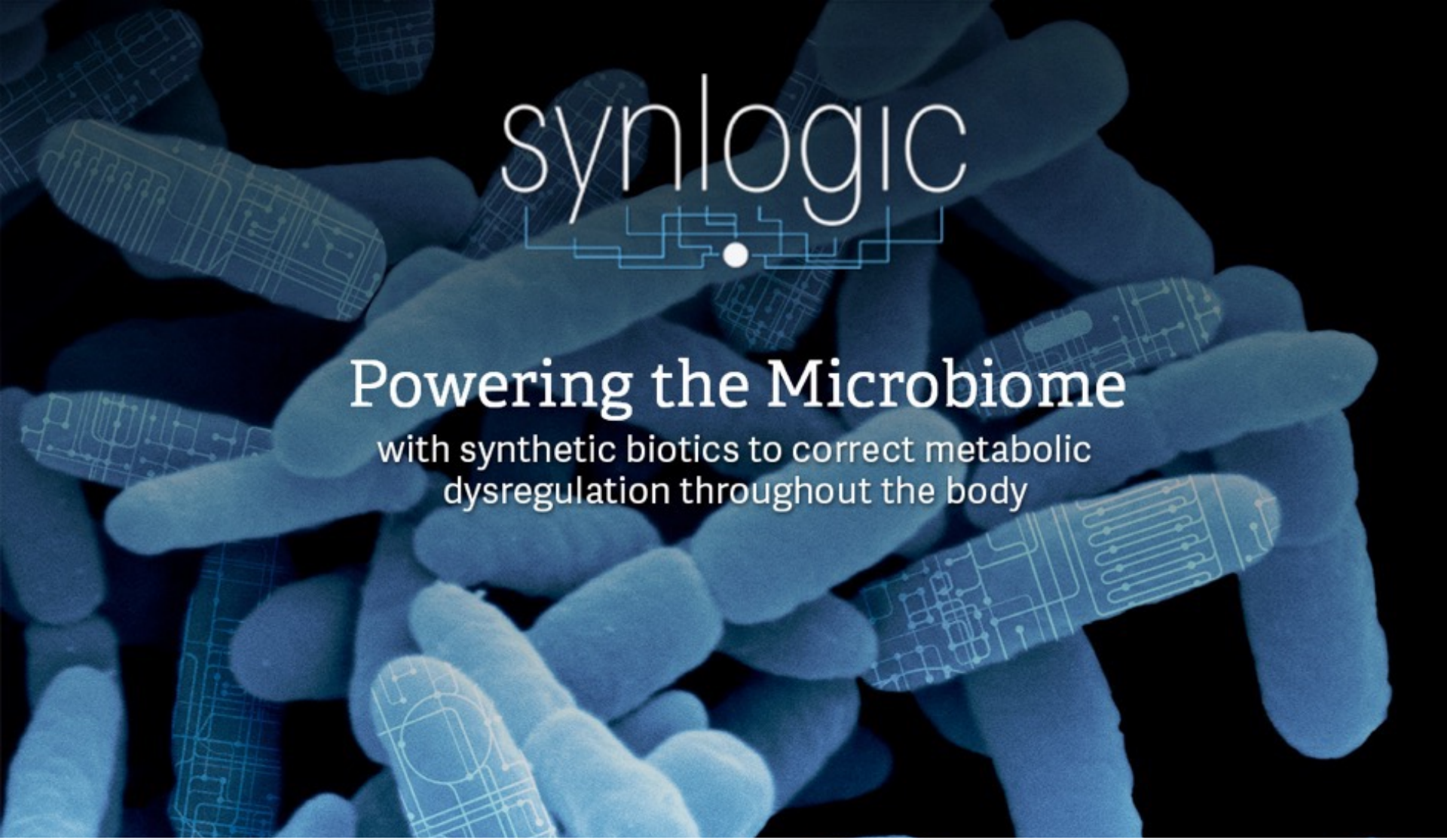
- **President:** Bharatt Chowrira (Auspex, Addex, Nektar, Merck, Sirna)

- **COO:** Alison Silva (TOG, Marina, Cequent, Pfizer)

- **CSO:** Paul Miller (AstraZeneca, Pfizer)

- **CTO:** Dean Falb (Stryker, Praecis, Millennium)

- **CMO:** Saurabh Saha (BioMed Valley Discoveries, Novartis Institutes for BioMedical Research)



Thank You.

www.synlogictx.com