

Neonatal Medical Device Innovation: From Concept to Commercialization

May 31, 2022

Janene H. Fuerch, MD FAAP

Clinical Assistant Professor

Stanford University School of Medicine

Agenda

- Describe how we are applying a needs-based innovation process to neonatal health technology innovation and research
- Provide insight into the Biodesign Process and demonstrate case examples
- Share lessons learned on the path of physician entrepreneurship

Disclosures

Company	Title	Financial COI
Novonate	Consulting Medical Director	Ownership
EMME	Co-Founder	Ownership
Equalize Health	Advisor	-
OvaryIt	Advisor	Ownership
Keriton	Advisor	Ownership
EmpoHealth	Advisor	Ownership
Avanos	Advisor	Consulting

Meandering Career Pathway

Global Health



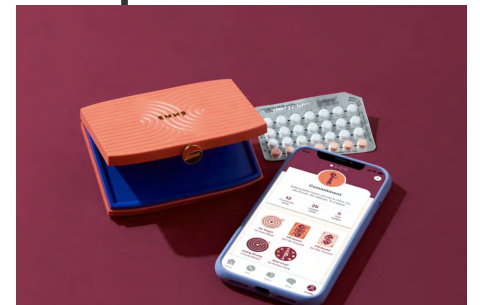
Innovation Fellowship



Simulation



Entrepreneurship



Clinical Research



Translation to Innovation

Equalize Health

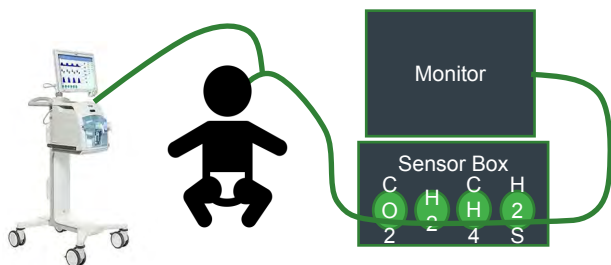


Figure 1: Prototype of D-Rev's novel CPAP

Biodesign Innovation Fellowship / Pediatric Health Technology Program



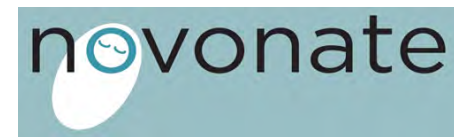
NEC Diagnostic



Epi Syringes

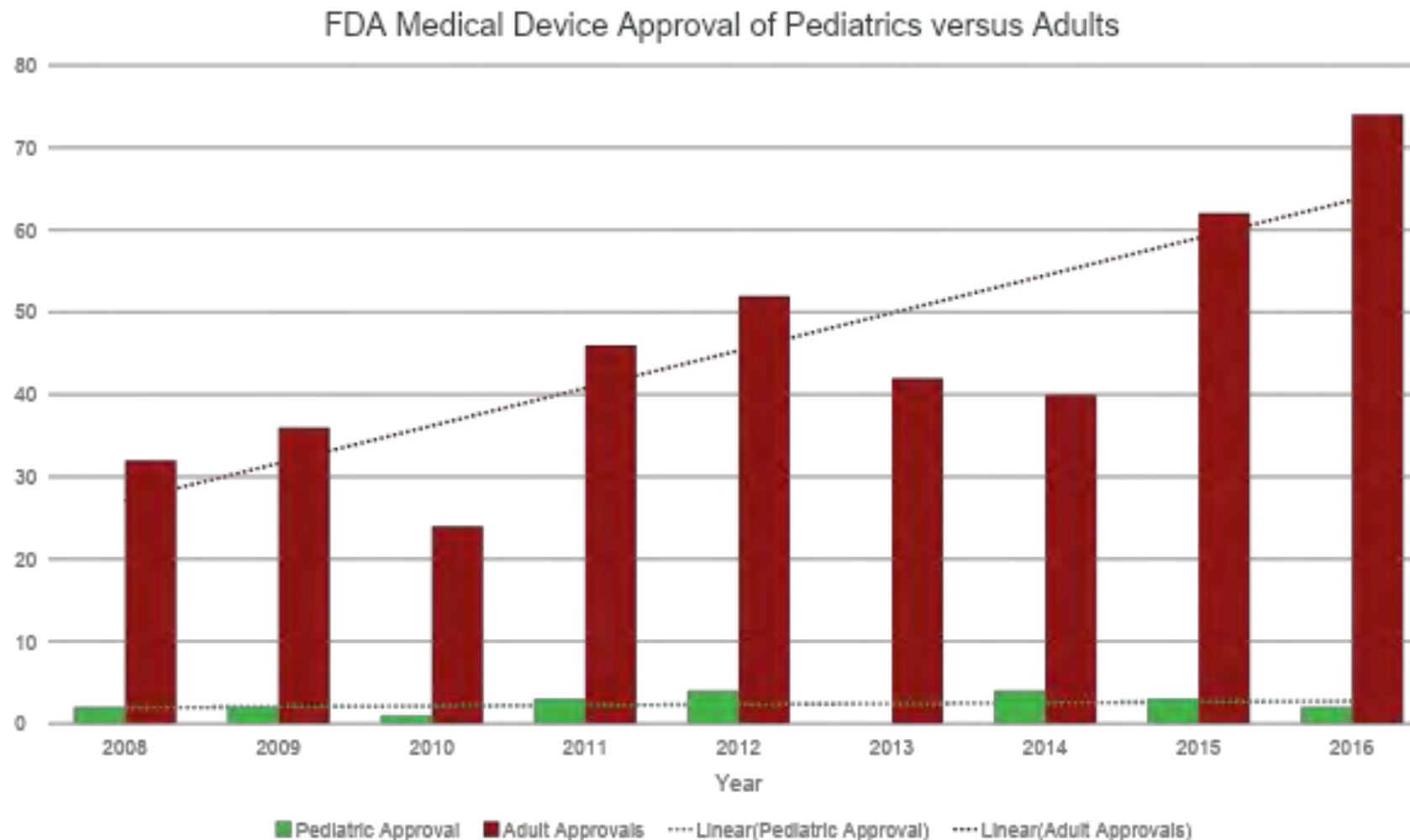


Company Development

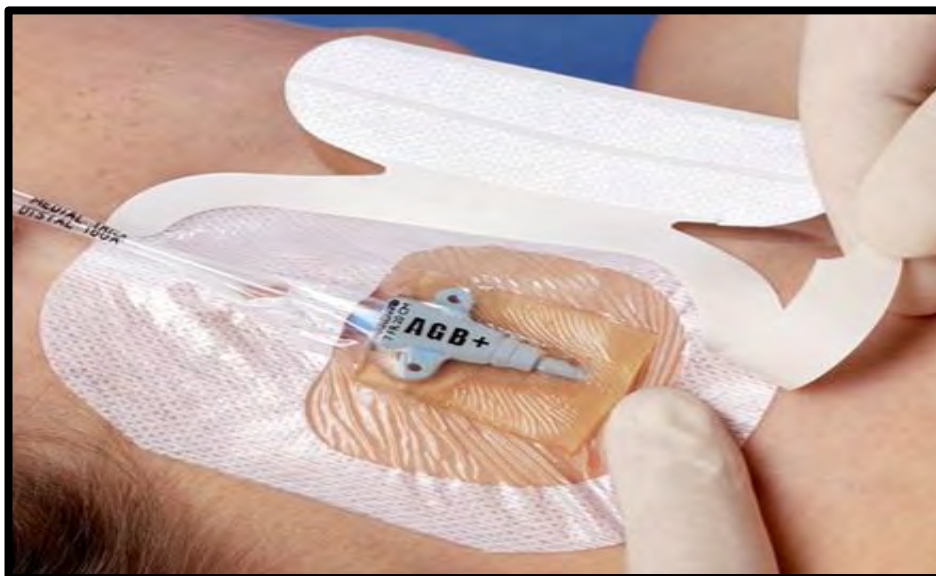


EMMÉ

Industry spends more money to develop health technologies that address the *last month of life* than on technologies that *can transform a lifetime*



A shocking inequity between adult and neonatal devices



Adult Central Line Management

- Protective
- Standardized
- Simple



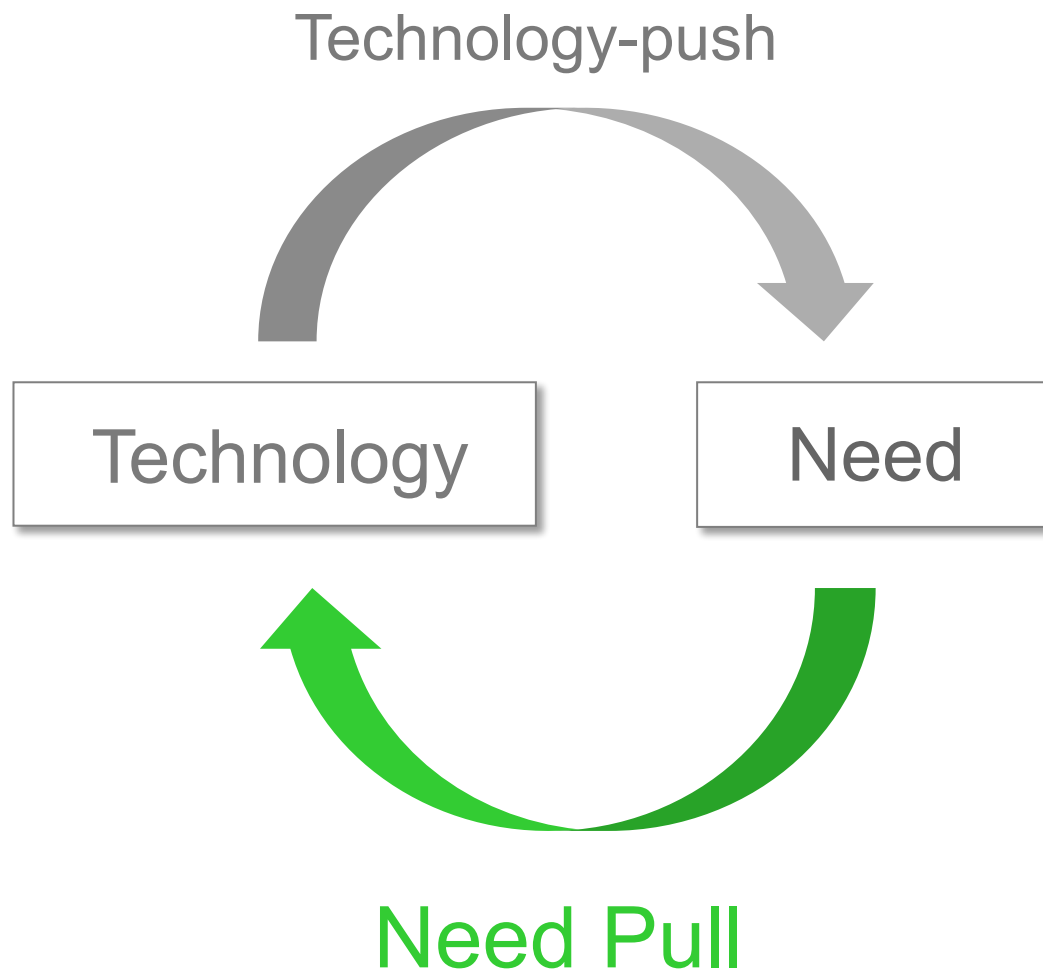
Neonatal Central Line Management

- Exposed
- Non-standardized
- Ineffective

We use medical devices every day, but rarely think about how they got there.



Innovation Approaches

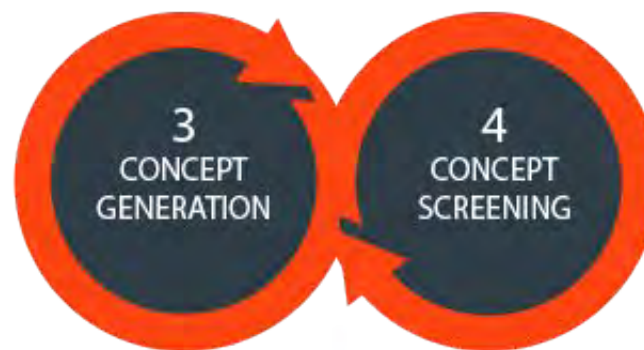


The Biodesign Process

IDENTIFY



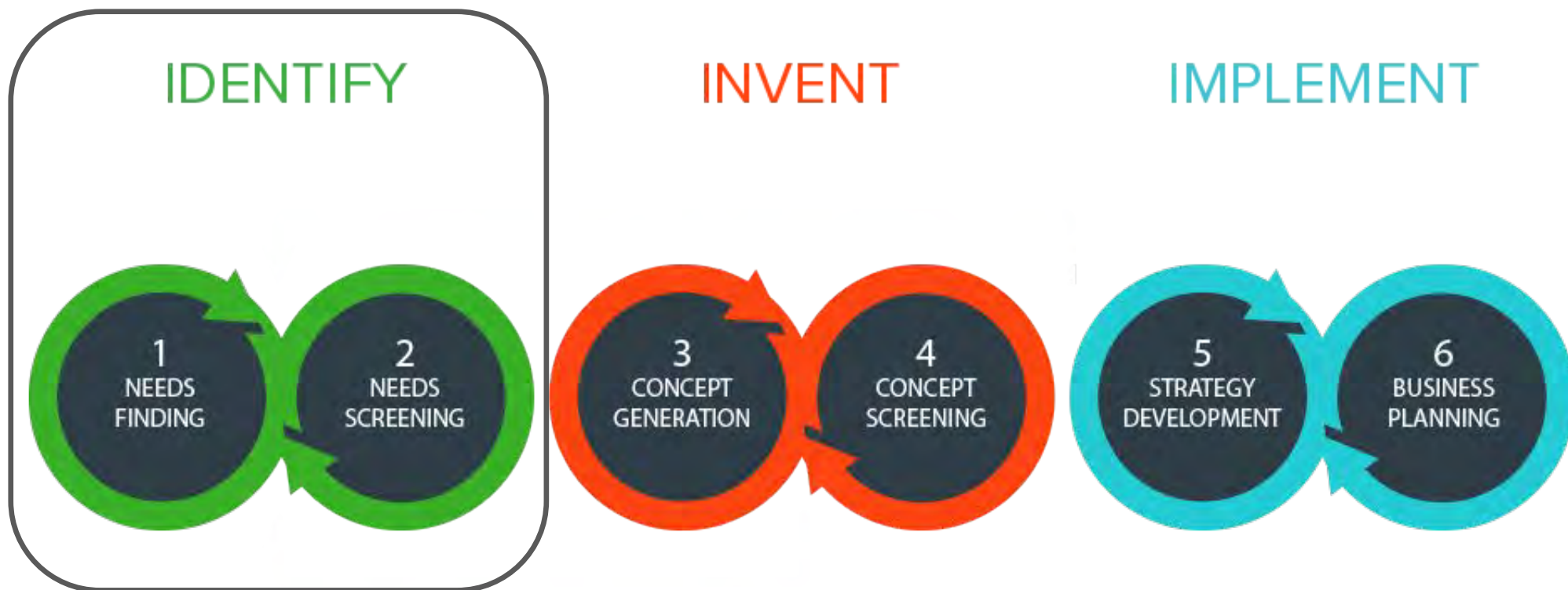
INVENT



IMPLEMENT



Stages 1 & 2: Needs Finding & Needs Screening



IDENTIFY



Need Statement

A way to [problem] in [population] in order to [outcome]

IDENTIFY



Need Statement

A way to [problem] in [population] in order to [outcome]

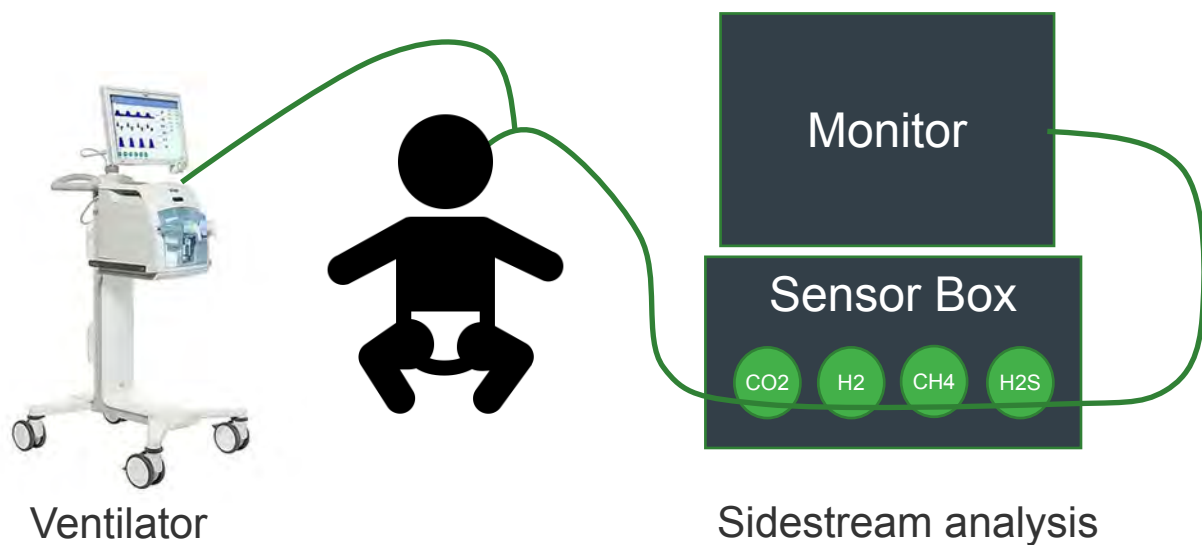
A way to detect harmful overgrowth of gut bacteria in hospitalized neonates receiving enteral feeds in order to prevent progression to surgical necrotizing enterocolitis.

IDENTIFY



NEC is hard to diagnose early

A breath-based, continuous monitoring device for necrotizing enterocolitis

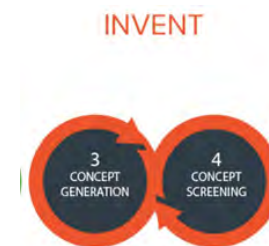
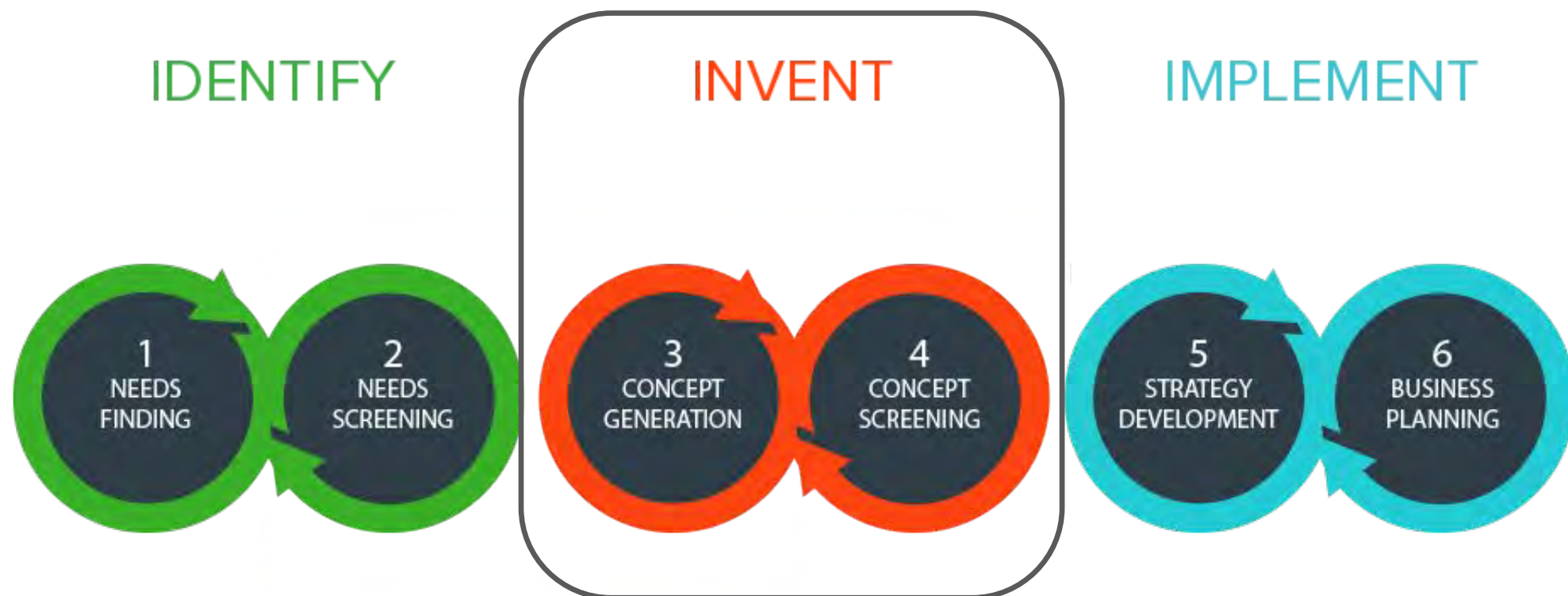


Exhaled breath from respiratory support device, delivered to analysis hardware

Impact

- 1) Diagnosing NEC early saves lives and prevents the need for more specialized care
- 2) Ruling out NEC allows for optimized patient nutrition and development

Stages 3 & 4: Concept Generation & Screening



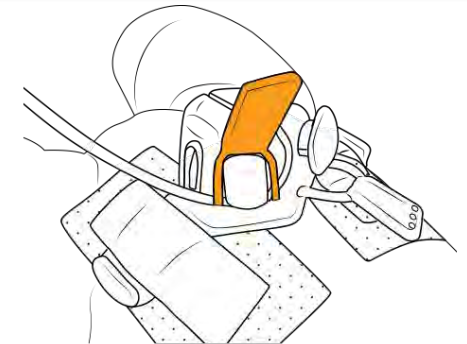
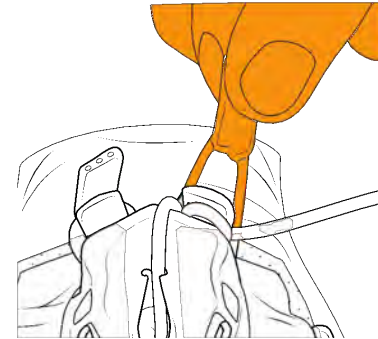
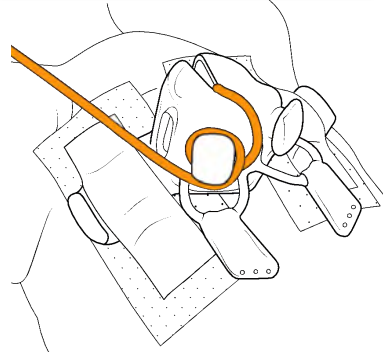
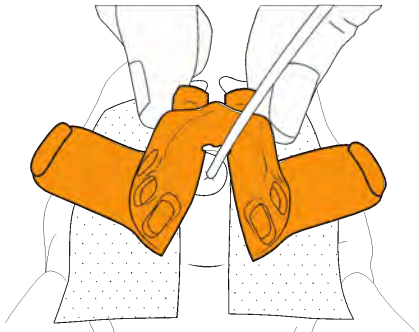
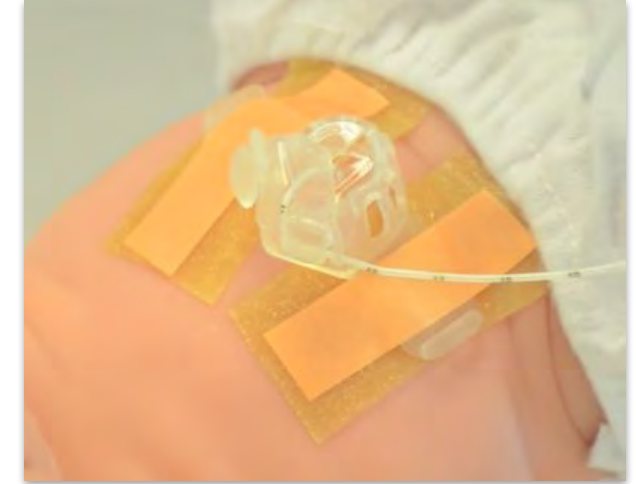
Need Statement

A way to [problem] in [population] in order to [outcome]

A way to protect umbilical catheters in neonates in order to decrease central line malposition and early removal.

INVENT



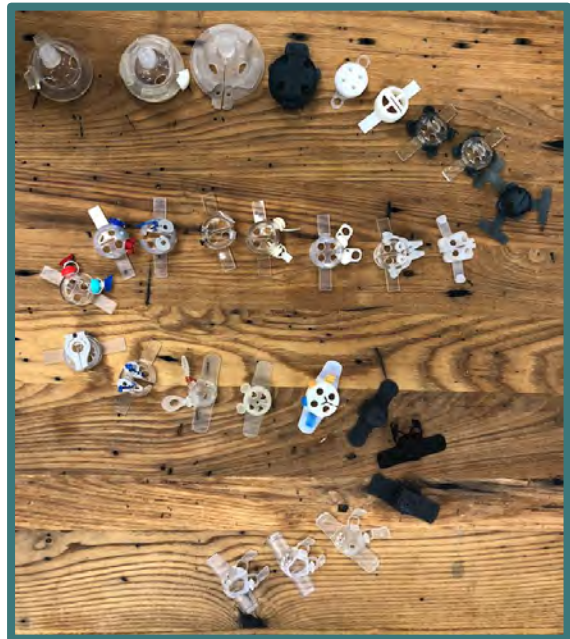


FDA registered & Commercially available
Supports 3.5 Fr to 5 Fr single and double lumen catheters
Can be used on neonates of all birthweights

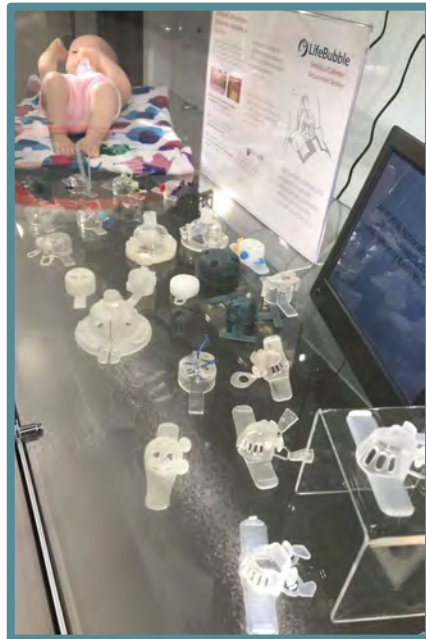
INVENT



Design Iteration from Testing



Biological



Catheter Securement



Fluid Flow

Nurse Interviews



INVENT



LifeBubble™

Umbilical catheter securement device

A New Method of Umbilical Catheter Securement Is Associated With Significantly Lower Rates of Malposition

Authors: Tanya Crabtree Beach MSN RN, Amy Olyaei BS, Brian Scottoline MD. PhD

Characteristic	Adhesive Control (AC) (n = 61)	LifeBubble (LB) (n = 58)	P value
Female	52.4%	41.4%	0.347 †
Birth weight, mean (range)	2281 g (1000, 4235)	2471 g (1000, 4830)	0.06 #
Gestational age at birth, mean (range)	32.9 wks (26.3, 40.7)	34.6 wks (26.8, 42.3)	0.132 #
Congenital heart disease	27.8%	46.6%	0.05 †
Umbilical catheters, total (UCs)	106	89	--
Patients with two umbilical lines	68.9%	53.4%	0.329 †
Patients with one umbilical line	31.1%	46.6%	0.124 †
Final placement firm	95%	88%	0.47 †
Central line associated blood stream infection (CLABSI)	0%	0%	--

Outcome Measure	Adhesive Control (AC) (57 UVC, 49 UAC)	LifeBubble (LB) (54 UVC, 35 UAC)	P value
Umbilical line moved more than one vertebral body	52.4%	12%	0.00001†
UVC movement	44.3%	5.6%	0.0000†
UVC discontinuation	39.3%	5.6%	0.00008†
UAC movement	29.5%	11.4%	0.106†
UAC discontinuation	7.4%	0%	0.20#



▶ **7X Reduction** in early UVC discontinuation due to malposition with LifeBubble

INVENT



Novonate Road Map



Stanford
Children's Health



**2 Med
Scholars +
3 eng. grad
students**

**\$88k
Coulter
grant
2015**

**\$50k
APDC
grant
3/2017**

**\$100k
invested
3/2017**

**\$225k
SBIR
grant
7/2017**

**1,000+
patients
2020-2022**

**R&D
Facilities +
Equipment**

**Access to
LPCH
NICU**

**2
people
Startx
Resources**

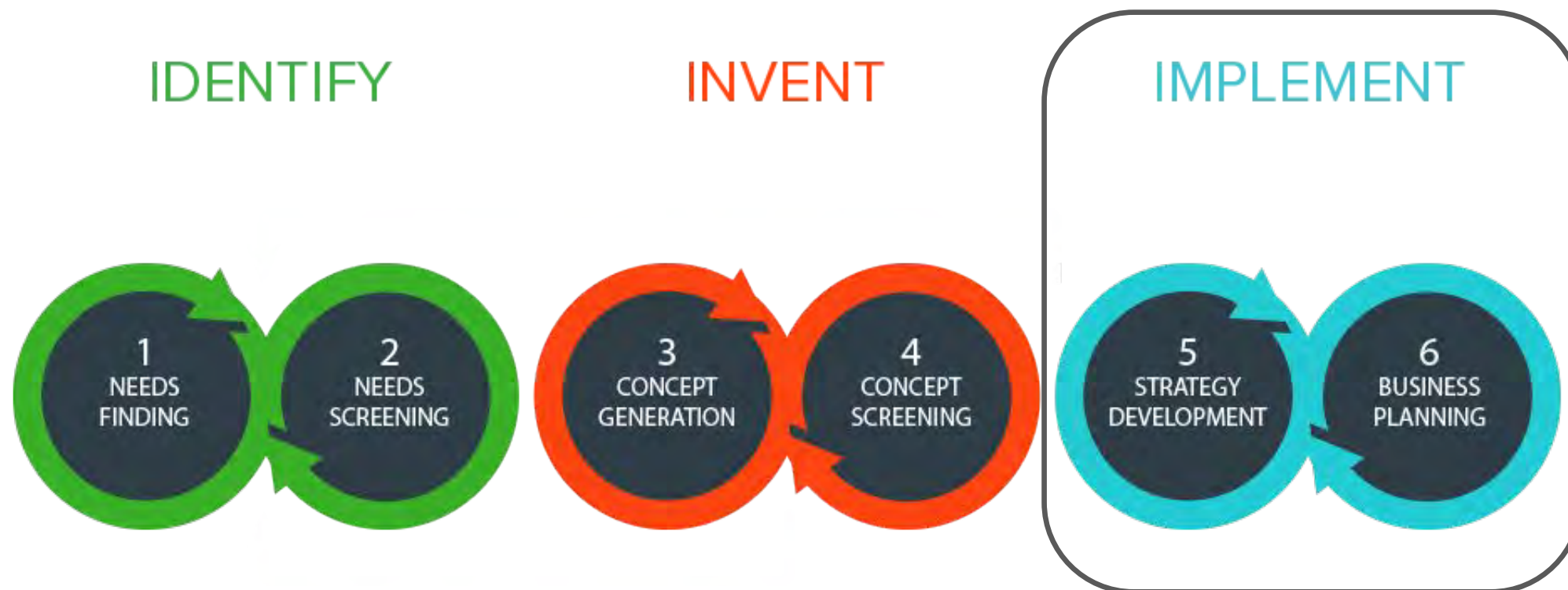
**5
Rosenman
Institute
Interns**

**\$1MM
Series
Seed
11/2017**

*Leveraged university and non-profit
resources as much as possible to reduce
risk and capital requirements*

MTVP | Medical Technology
Venture Partners

Stages 5 & 6: Implementation Planning



IMPLEMENT



NEED STATEMENT:

A way to improve adherence for oral contraceptive pill (OCP) users who are trying to prevent pregnancy to reduce the number of missed pills per cycle.



IMPLEMENT



The EMME Experience



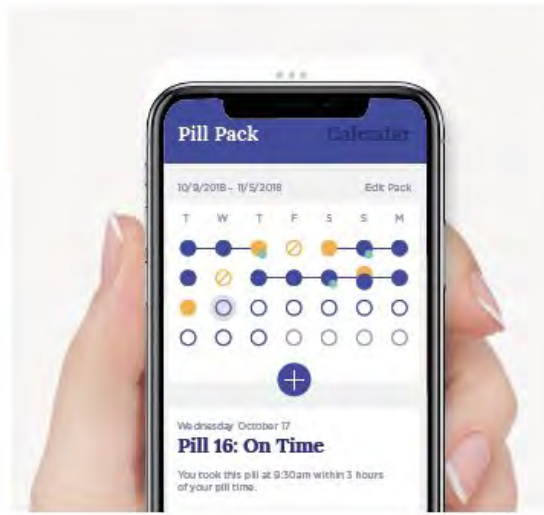
Join

Become an EMME member, get Rx if needed, and become part of a sisterhood



Rx + Case

Get birth control + EMME case by mail, all in one easy starter kit



App

Case tracks pills and syncs with app to offer daily personalized reminders and insights



Refills + Telemedicine

EMME uses data to send perfectly timed monthly refills and enhance telemedicine experience



Positive Outcomes

Connected tracking enables positive outcomes for women's health

1



2



3



4



5



TM
EMMÉ

I hereby certify that this correspondence is being filed via EFS-Web with the United States Patent and Trademark Office on January 7, 2018
Jyoti Khader

PATENT
 Attorney Docket No.: 52844-703.201

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Amanda B. French et al.

Application No.: 15/950,059

Filed: April 10, 2018

For: METHOD AND SYSTEM FOR IMPROVING AND ASSISTING IN MEDICATION COMPLIANCE

Customer No.: 21971

Confirmation No.: 3950

Examiner: ALIZADA, Omeed

Art Unit: 2684

PETITION TO REVIVE UNINTENTIONALLY ABANDONED APPLICATION

Intellectual Property

Patent granted in 2021

Regulatory

Class I device
 Quality system
 Registered with FDA

Reimbursement

Self-pay FSA
 Insurance coverage

Business Model

B:C
 B:B
 Insurers

IMPLEMENT



Never Miss a Dose

Emme Smart Birth Control System



IMPLEMENT



Successful Pediatric Devices

An emerging track record of venture capital backed companies and acquisitions

Clinical Needs

Solutions

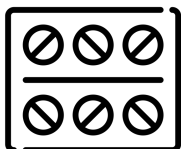
Companies



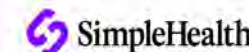
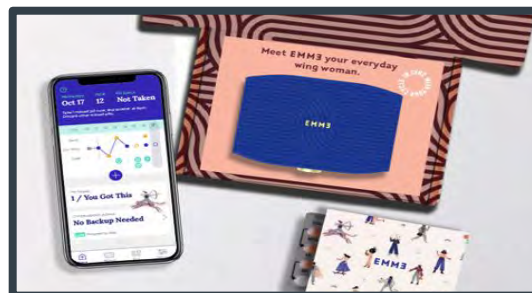
Inadequate protection of neonatal central lines



Umbilical Catheter Protection
 Raised \$1M, Commercially available, Acquisition talks



Unwanted pregnancies while on OCPs



Managing Life on the Pill
 Raised \$3.5M, Commercially available



Impractical home asthma monitoring



TUEOHEALTH
Home Asthma Management
 Raised \$1.1M, Acquired by Apple



Unique Challenges in Pediatrics

- Orphan indication
 - small market size
 - few institutional investors



Funding

- Growth
- Subpopulations
- Smaller scale
- Discomfort tolerability



Engineering

- Burden of evidence for FDA approval
- Life-long injury risk

Regulatory



Ethics



- Potential to harm
- Inability to self-advocate

Vision

*To be a global leader in pediatric health technology innovation
to improve lives everywhere*

Solution

*Incubate promising technologies to
develop translatable health technologies for children*

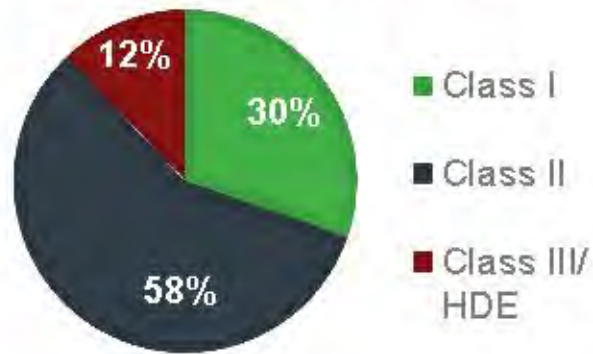




Pediatric Health Technology Program

Stanford Biodesign - 2021 Recap

Device Classifications



\$400,000 awarded with UCSF to **10** pitch winners



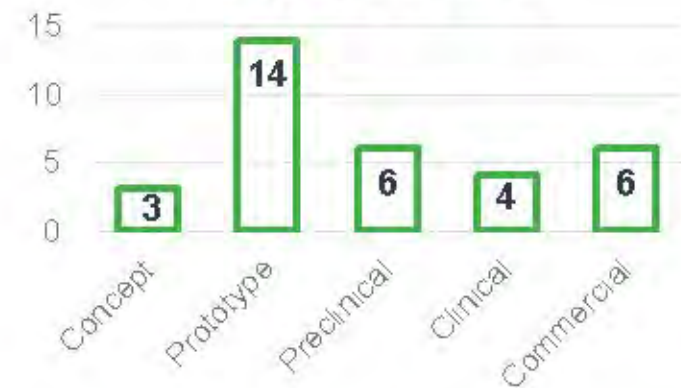
Over **\$75,000** granted to **6** projects following coaching



Policy initiative launched to address development barriers



Project Phases



Stanford PHTP projects from 2019 - 2021 have:



Impacted over **18,100** patients



Raised **\$41.6M** through grants, venture and angel investments

Accelerator Pitch Competition – JOIN US!

UCSF–STANFORD
Pediatric Device Consortium

Pediatric Device Accelerator Pitch Competition 2021
\$400,000 in funding available for your device projects!



October 7, 2022

- 10-12 teams competing for \$400,000 in grant funding
- Grand Prize \$100,000
- *2022 Winner: Radiant Oximetry*
- *2021 Winner: Novonate*
- *2020 Winner: Eclipse Regeneration to treat Short Bowel Syndrome*

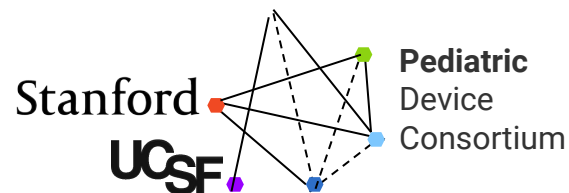
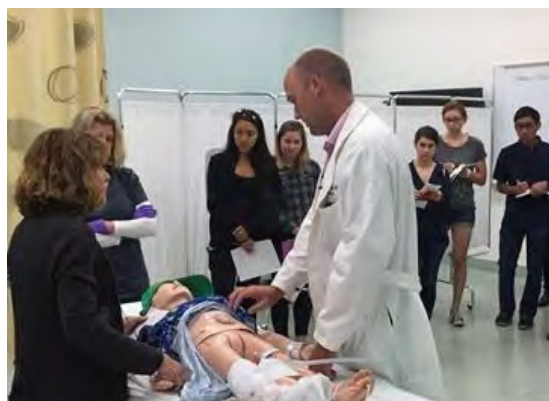
www.PediatricDeviceConsortium.org

Some Alternative Careers

- Academic research
- Scientist translating technologies
- Industry trials
- Biotech / Medtech
- Angel investing / Venture capital
- Consultant
- Advisor
- Entrepreneur

Interested and want to learn more?

Contact:
jfuerch@stanford.edu



STANFORD BYERS CENTER FOR
BIODESIGN

ASCEND



Maternal & Child Health Research Institute



Creating Your Biotech Startup

Entrepreneurship and Innovation in Medicine

May 31 2022

C. Vivek Lal, MD, FAAP

Associate Professor

Director, Lung Microbiome Lab

University of Alabama at Birmingham, AL

Founder, Biostack Ventures

ResBiotic, Inc. and Alveolus Bio, Inc.



What is Innovation



Innovation is the process of doing something new, different, smarter or better that will make a positive impact

The My Why ?



Why Medical School ?

Impact in
Healthcare



Why Residency Training ?

Impact in
Healthcare



Why Fellowship Training ?

Impact in
Healthcare



Why Research Track
Faculty Appointment ?

Impact in
Healthcare



Why Academic
Entrepreneurship &
Innovation ?

Impact in
Healthcare

Basic Foundations: Introduction to Research in Lung Biology

UT Southwestern
Medical Center



Margaret Schwarz, MD



Rashmin Savani, MBChB



Philip Shaul, MD

Birth Defects
Research
Part A

**Clinical and Molecular
Teratology**

Research Article

Vascular mediators in chronic lung disease of infancy: Role of endothelial monocyte activating polypeptide II (EMAP II)

Charitharth Vivek Lal, Margaret A. Schwarz

American Journal of Respiratory Cell and Molecular Biology

Home > American Journal of Respiratory Cell and Molecular Biology > List of Issues > Volume 55, Issue 4

Endothelial Monocyte-Activating Polypeptide II Mediates Macrophage Migration in the Development of Hyperoxia-Induced Lung Disease of Prematurity

Daniel D. Lee ^{1*}, Charitharth V. Lal ^{2,3*}, Elizabeth A. Persad ³, Chinn-Woan Lowe ¹, Anna M. Schwarz ³, Niranjan Awasthi ³, Roderich E. Schwarz ^{4,5}, and Margaret A. Schwarz ¹

+ Author Affiliations

Novel Foundations: Systems Biology Approach; Introduction to OMICS

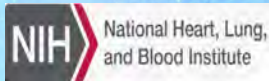
UAB THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM



Namasivayam
Ambalavanan, MD

Creating Your Niche: Microbiome of Lung Diseases

Started Pulmonary Microbiome
Lab at UAB



UAB THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM



Ed Blalock, PhD



Amit Gagar, MD,
PhD

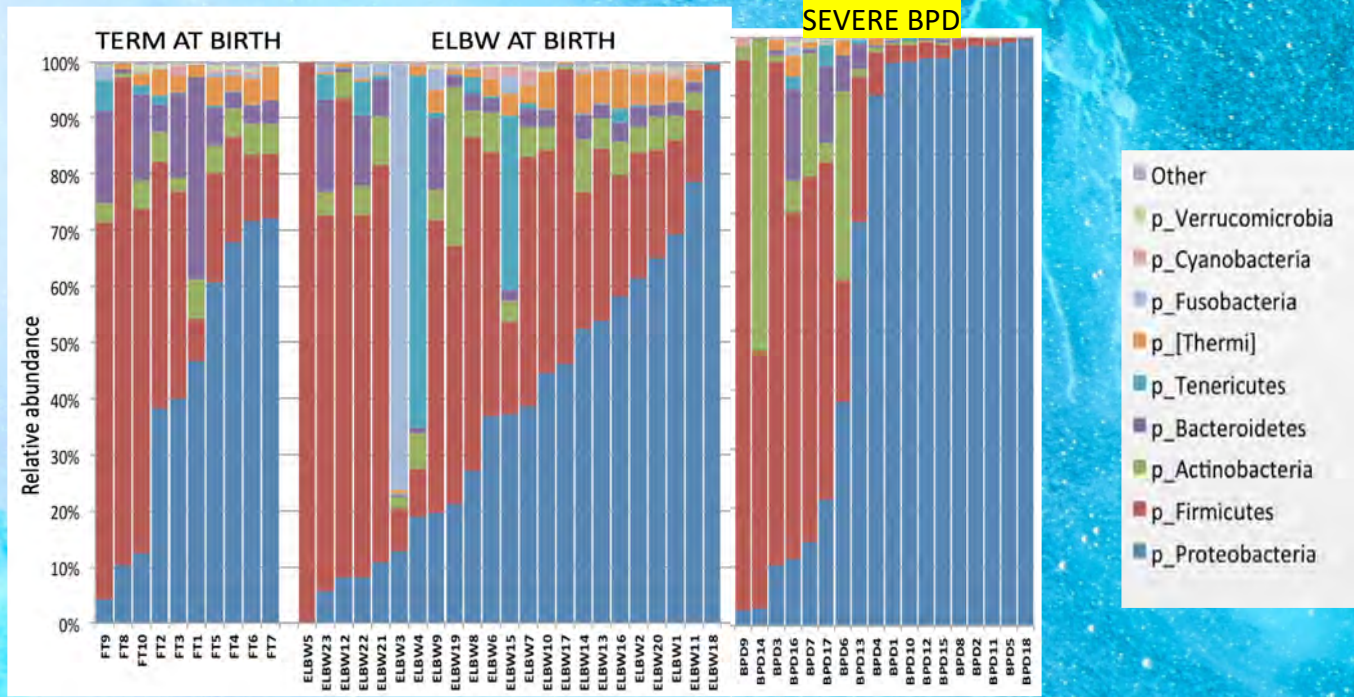


Namasivayam
Ambalavanan, MD

Observations From the Bedside: Infant Airway Microbiome Study; 2014-15

- Prospective cohort study of all intubated preterm infants (<28 weeks) gestation and full-term infants (37 weeks)
- Tracheal aspirates (TA) at birth (or within 6 hrs) and various time points were collected
- Discovery cohort, and a Validation cohort (total n=150)
- 16s rRNA microbiome analysis

Distinct Microbiome Signature in Infants with Severe BPD



From Bedside to Bench; 2015-2019



Kalsang Dolma, MD



Amelia Freeman, MD



Sam Gentle, MD



Teodora Nicola, MD, PhD



Gabriel Rezonzew, MD



Luhua Qiao, MS



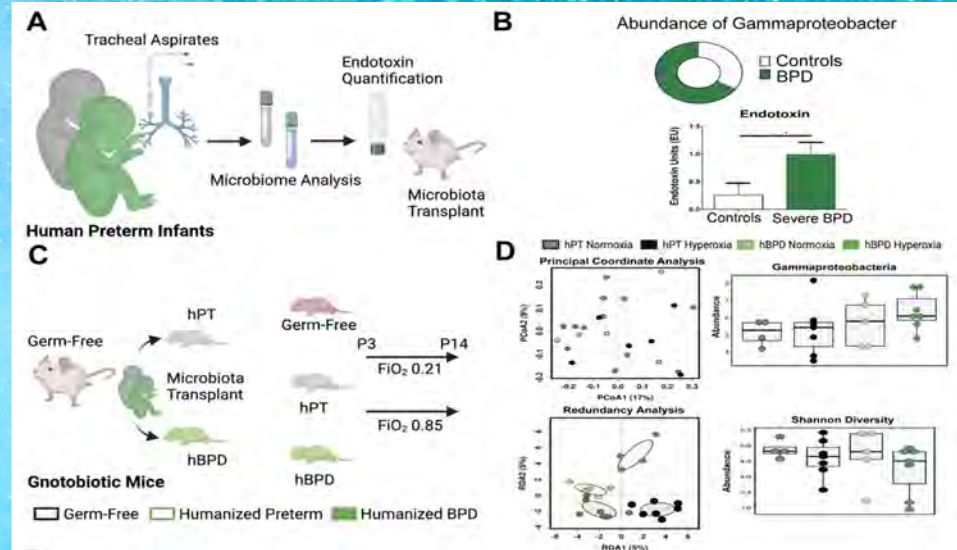
Trent Tipple, MD



Rakesh Patel, MD



Kent Willis, MD



Dolma et al, *AJP Lung*
 Lal et al., *JCI Insight*
 Genchmer et al., *Cell*

Freeman et al., *Resp Research*
 *Freeman et al. in revisions
 *Nicola et al. in submission
 *Wenger et al. in submission
 *Qiao et al. in submission
 *Rezonzew et al. in submission

*Delayed publication due to IP reasons

Back to Bedside - Birth of Biotech Startups; 2020-21

Alveolus™

 **ResBiotic™**

UAB BILL L. HARBERT INSTITUTE FOR
INNOVATION AND ENTREPRENEURSHIP

The University of Alabama at Birmingham

Why Start a Company ?

Fill Market Need

Financial
Returns

Organization
Inventor
Management

Potential for
Societal Impact
and Helping
Others

Challenges in Academic Entrepreneurship

Information
and Cultural
Barriers
Between
Academics and
Industry

Inadequate
Organizational
Resources
esp. in Tech
Transfer
Offices

Inadequate
Training for
Faculty in
Entrepreneurial
Process

Traditionally
Insufficient
Reward for
Faculty
Entrepreneurial
Activity

Conflict of
Interest &
External
Activities

Conflict of
Commitment

State Laws

Indicators of Performance

Traditional Academics

Quality of Clinical Care
Clinical Revenue
Patient Advocacy
Education
Research Manuscripts
Extramural Research Funding
Leadership
Mentoring

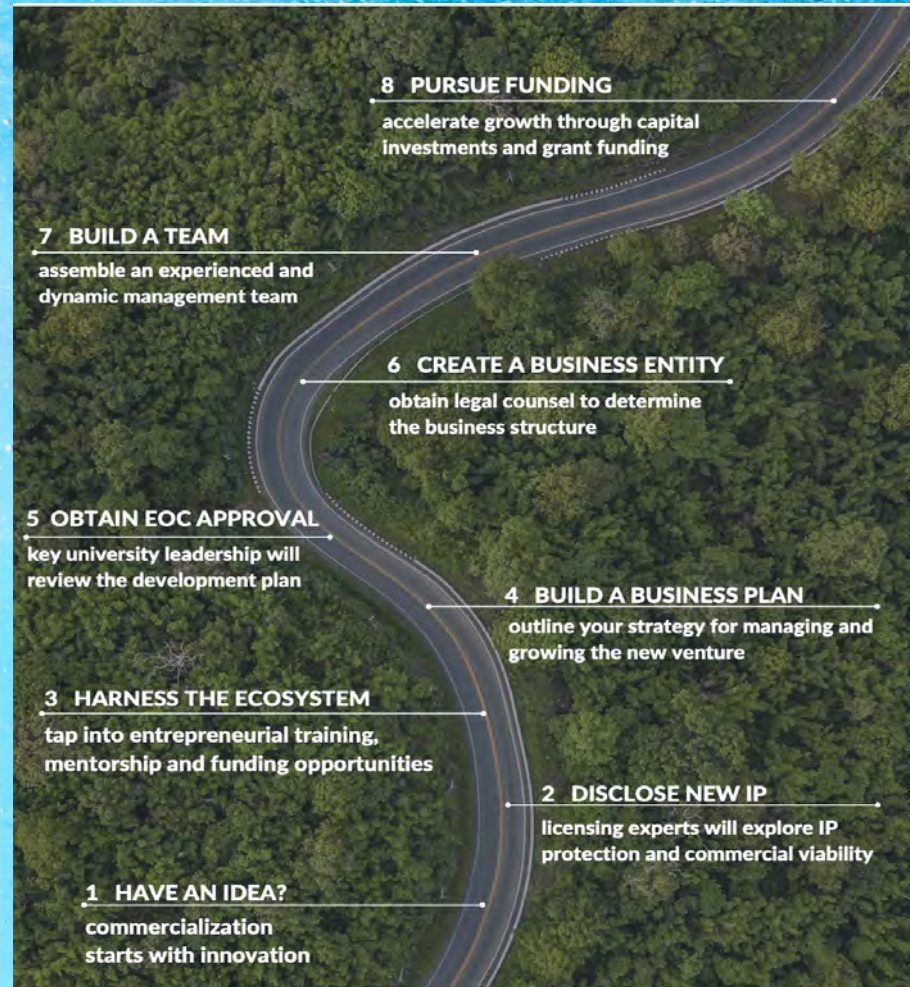
Entrepreneurial Academics

All Traditional Academic Metrics, plus:

Invention Disclosures
Patents
No. of Licensing Agreements
Licensing/IP Revenue
Startup Formation
Startup Survival
Employment Growth

The Startup Innovation Roadmap

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The University of Alabama at Birmingham

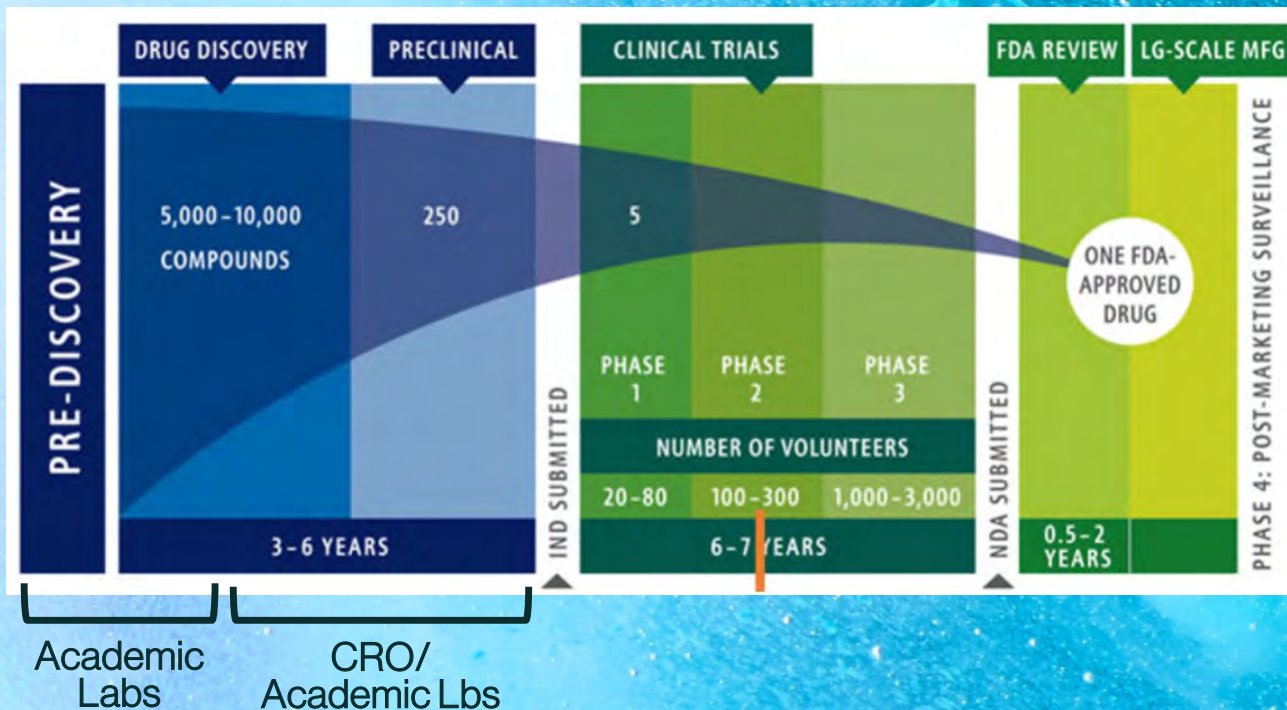


The Key Ingredients (to get started...)





Drug Discovery Timeline



Critical Steps After Academic Discovery

API/Drug Product Definition

Repeat the Efficacy Study
Active Substance Analysis (Secretome Analysis)
General Mechanism of Action Studies

Chemistry, Manufacturing and Controls (CMC)

API Process Development & Representative Batch for Preclinical
Get Drug Product Vendor in Place
Drug Product Development & Representative Batch for Preclinical
Get Analytical Vendor in Place (if not same as API or DP vendor)
Analytical Method Development
API Characterization & Stability
Product Characterization & Stability
GMP API mfg, release & stability
GMP Product mfg, release & stability
GMP Product Labeling and Distribution to Site
COGS analysis

Preclinical Studies

Get Bioanalytical Vendor in Place
Bioanalytical Method Development
Determine Required Pharmacology Studies - May need more than 1 animal model
Get Preclinical Vendor in Place (if not same as Bioanalytical vendor)
Repeated Dose analysis, recovery + Biodistribution?
Biodistribution (e.g. lung, mouth, sinus, gut, eyes + Required Organs)
GLP Bioanalytical Method Qualification
GLP Single Dose Ranging Toxicology
GLP Repeated Dose Toxicology (+ Ophthalm & Recovery)
GLP Single Dose Resp Safety Pharmacology

Clinical Strategy

Assay Development and Validation
Identifying Phase 1 to Phase 3 Studies that would be conducted
Identifying details of end points, patient populations
Identifying dose selection, timelines, developmental costs
Detailed protocols

Regulatory

Get Regulatory Vendor in Place
Notify FDA Division PM of intent to submit Pre-IND Request
Submit Pre-IND Request Letter
Prepare Pre-IND Briefing Package (start as early as feasible)
Submit Pre-IND Briefing Package
Pre-IND "Meeting" (may just be written comments from FDA)
Pre-IND Sponsor response to FDA comments
Pre-IND Final Meeting Minutes from FDA
Prepare IND
Submit IND
FDA Study May Proceed / Hold

Global Respiratory Disease Market Over \$100B

15.7M Americans suffer from COPD.

6.2M Americans suffer from late-stage, high exacerbating COPD

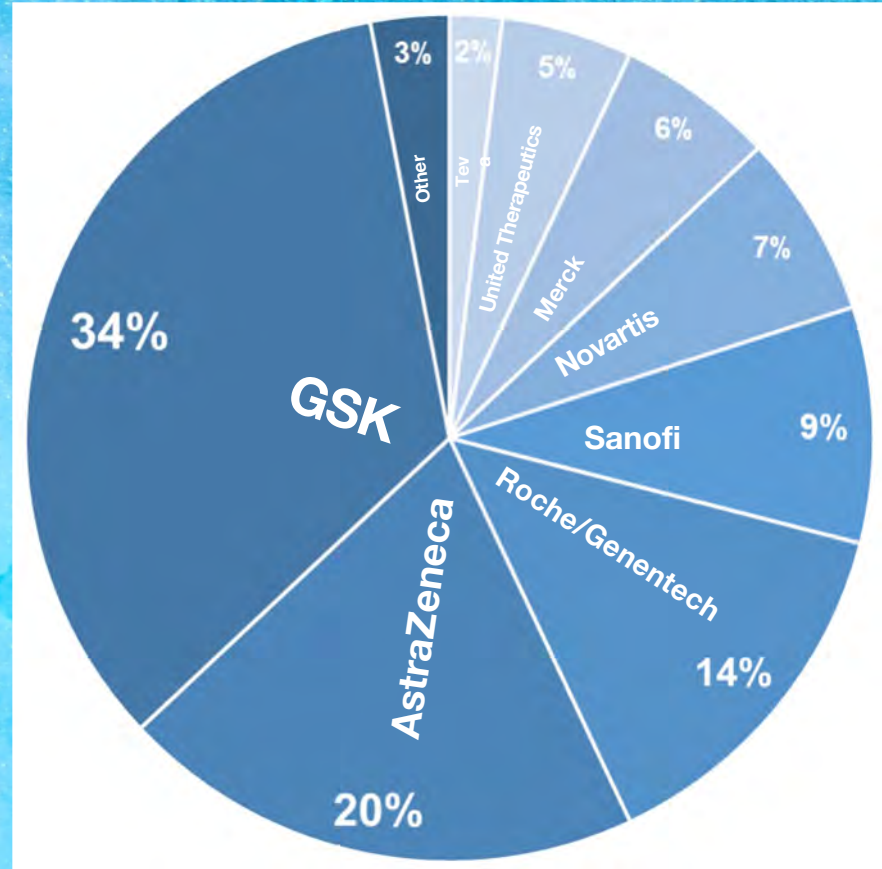
65M COPD patients globally and rising

Viral illnesses are pervasive and have long-term costs beyond initial treatment.

~2M influenza illnesses/year in US

430M COVID cases globally and rising

Bronchopulmonary Dysplasia: 10-15k patients per year



A High Growth Opportunity: Everyday Lung Health



Relief Seekers

> 70M People (US)

- ~ 24M Americans are living with COPD¹
- ~ 25M Americans are living with Asthma²
- ~ 24M Americans experience allergic rhinitis (hay fever)³



> 150M People (US)

- ~ 135M Americans live in an area where monitors that are capturing unhealthy levels of ozone or particle pollution⁴
- ~ 50M Americans experienced dangerous air quality in 2020 due to wildfires alone⁵



Athletic Optimizers

> 80M People (US)

- ~ 60M Americans participate in running and jogging⁶
- ~ 27M Americans swim for fitness⁷



The Healthy-ish

> 50M People (US)

- ~ 8.1M Americans use e-cigarettes⁸
- ~ 48M Used marijuana at least once in 2019⁹

A Whole New Class of Probiotics

*Clinically studied
probiotic strains*



Bioactive botanicals

Vasaka, Turmeric,
and Holy Basil

Developed by leading physician scientists

Disrupting a brand-focused industry with
a clinically validated solution

Based on over a decade of research at
major research universities

Supported by a team of internationally
renowned scientists and advisors

Empowering a growing market of
consumers with a simple and science-
backed approach to everyday lung health

*In the
News*

MicrobiomeTimes



Flagship Formula

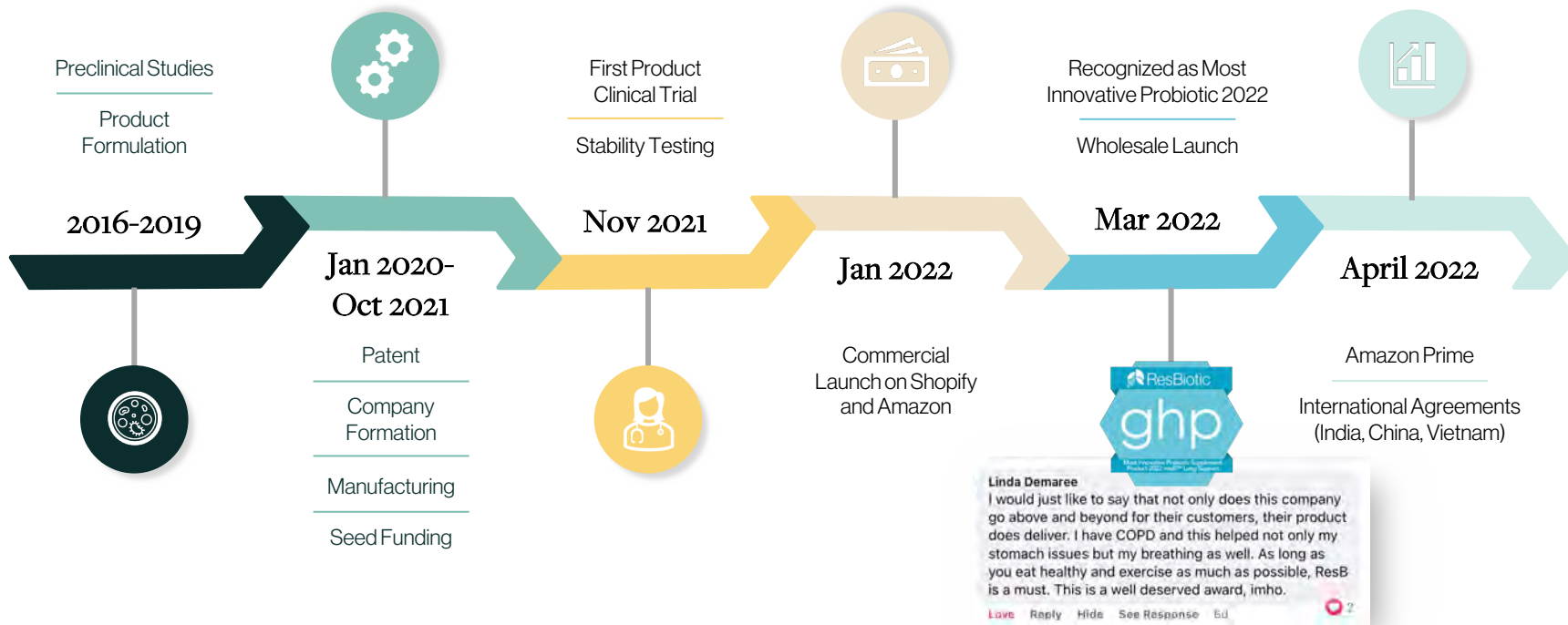
*for Digestion, Immune Function,
& Respiratory Health*



\$59
per bottle

- **Unique, proprietary formula**
- Ingredients backed by **100+ clinical studies**
- **Clinically studied product** in healthy adults, adults with asthma, and smokers (publication pending)
- **Stable** at room temperature
- Third party tested

Launching resB™ Lung Support



Alveolus Core Team



C. Vivek Lal MBBS, MD, FAAP

Chief Executive Officer, Founder
ICU physician, lung microbiome expert, serial entrepreneur



Andrew O' Connor MS, MBA

Chief Operating Officer
Respiratory particle engineer, VC at Morningside Ventures, In-Q-Tel B.Next



Amit Gaggar MD, PhD

Chief Medical Officer
Pulmonologist, cystic fibrosis and COPD expert



UNIVERSITÄT
HEIDELBERG
ZUKUNFT
SEIT 1386



Teodora Nicola MD, PhD, MBA

Lead Scientist
Lung molecular biologist, lung & cancer disease model expert, 20 years of research management



Winston Gu PhD, MBA

Senior Scientist
In vitro mechanistic expert with microbiology and translational science expertise

ResBiotic Core Team



Dr. Vivek Lal
Chief Executive Officer

UT Southwestern
Medical Center



Nina Rance
Chief of Staff

WELLESLEY



Maggie Belshé
Chief Customer Officer

BARNARD
BARNARD COLLEGE - COLUMBIA UNIVERSITY



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Advisor – Respiratory Toxicology,
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Rakesh Patel, PhD
Advisor – Inflammation, Pulmonary
Hypertension; Vice Chair, Research – UAB

Partnerships



Other members:

Other members:



Johnson & Johnson



The background of the slide is a photograph of several jellyfish swimming in clear, blue water. The jellyfish are translucent with visible internal structures and are scattered across the frame. The lighting is bright, creating a vibrant blue color palette.

Interested in Learning More ?

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