HARVARD UNDERGRADUATE CBE

Exploring the Microbiome and the Gut-Brain Axis

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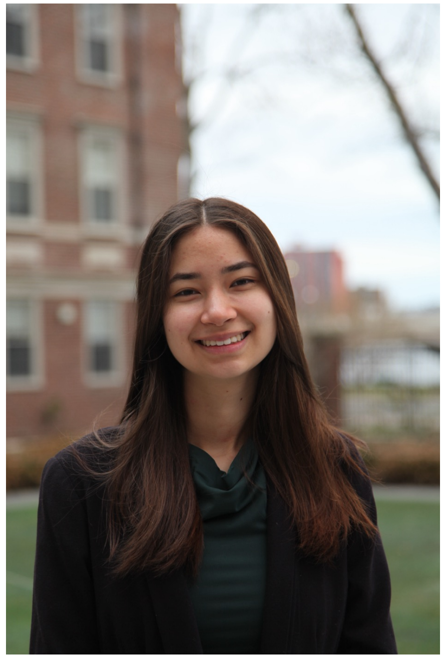
Team Introduction

The Microbiome Life Sciences Think Tank is composed of five HUCBE members with a diverse range of backgrounds and a shared interest in the life sciences. This deliverable is the result of eight weeks of research exploring the microbiome.



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Project Overview

Over the course of eight weeks, our team investigated the gut microbiome, the gut-brain axis, and their current and future impact as commercial products such as biomedical therapeutics, cosmetic supplements, health surveillance tools and more.

After thoroughly analyzing current major players in the microbiome market, synthesizing ongoing scientific research, and conducting interviews with industry professionals, the team identified promising areas of growth and outlined strategic considerations for a potential startup interested in making a splash in the microbiome market.

Section 1: Microbiome and Gut-Brain Axis Overview

Section 2: Market Overview and Competitor Analysis

Section 3: Emerging Opportunities for Commercialization

Section 4: Key Strategic Considerations

Section 5: Expert Interviews

Microbiome and Gut-Brain Axis Overview

This section provides a deep dive into the scientific background of the digestive system and gut microbiome, as well as its effects on the rest of the body, including the immune system and the brain.

Overview: The Human Gut Microbiome

The human body consists of many distinct microbiomes, and the gut microbiome is the most important and well-researched. It serves important metabolic functions and influences many body systems, including the digestive system.

Human Microbiome

- The **human microbiota** refers to the **microbial taxa** inhabiting humans, and the **microbiome** refers to the **catalog** of these microbiomes and their genes.
- While there are a few prominent patterns, every individual has a **unique microbiota profile** influenced by their **environment and lifestyle**.
- There are many **distinct human microbiomes** found on the skin, in the mouth, and more, but **most influential** to human health is the **gut microbiome**.

Gut Microbiome

- The human GI tract contains around **100 trillion microbes**, inhabiting one of the **densest habitats on Earth** at a density of around 1010 cells per milliliter.
- The gut microbiome contains bacteria, archaea, fungi, parasites, and viruses.
- Phyla **Firmicutes and Bacteroidetes** account for 90% of the gut microbiota, and ***Clostridium*** accounts for about 95% of the Firmicutes phylum, followed by genera *Bacillus*, *Enterococcus*, *Lactobacillus,* and *Ruminicoccus*. Bacteroidetes consists of predominant genera such as *Bacteroides* and *Prevotella*.
- The gut microbiome aids in **metabolism** by **digesting** complex **carbohydrates** and **dietary fibers** into short-chain fatty acid by-product and **providing enzymes** used to synthesize vitamins like B1, B9, B12, and K.
- Gut bacteria are also important in the **breaking down**, **reabsorption**, and **recycling of bile** from the intestines to the liver in **enterohepatic circulation**.

Organ	Movement	Digestive Liquids	Food Broken Down
Mouth	Chewing	Saliva	Starches
Esophagus	Peristalsis	None	None
Stomach	Upper muscles in stomach relaxes to let food enter, and lower muscle mixes food with digestive juice	Stomach acid and digestive enzymes	Proteins
Small Intestine	Peristalsis	Small intestine and digestive juice	Starches, proteins, and carbohydrates
Pancreas	None	Pancreatic juice	Carbohydrates, fats, proteins
Liver	None	Bile	Fats
Large Intestine	Peristalsis	None	Bacteria in the large intestine can also break down food

Cleveland Clinic (I), Cleveland Clinic (II), Cleveland Clinic (III), Duke, Gut Microbes, Microorganisms, NIDDK, UChicago

Overview: Neuroscience and the Brain

The human nervous system is a complex network, orchestrating bodily functions through neurons and neurotransmitters; the proper functioning of its physical components, interacting with the endocrine system, is essential to proper health.

Examples of Neurotransmitters

- **Acetylcholine**, a small-molecule transmitter in muscles, passes signals from **neurons** to **muscle** fibers. It also helps to **guide attention** and facilitate **neuroplasticity** across the brain.
- Mammals discharge **dopamine** in response to a **reward**. It is linked with motivation, decisions, movement, learning, memory and attention.
- **Norepinephrine** is a hormone and neurotransmitter, also called **noradrenaline**. It is linked to mood, **awareness**, memory, and **stress**.

Common Brain Conditions Involving Neurotransmitters

- **Reduced levels** of neurotransmitters such as serotonin, dopamine, and glutamate have been linked to various **depressive symptoms**.
- **Progressive dopamine deficits**, as well as dysfunction with serotonin, acetylcholine, and norepinephrine, are linked with **Parkinson's Disease**. Parkinson's Disease is a neurological movement disorder that worsens over time.

What is the Nervous System?	The nervous system has two main divisions: the **central nervous system** (CNS), which is the brain and spinal cord, and the **peripheral nervous system** (PNS), the nerves lying outside the CNS. It **controls bodily functions** like movement, breathing, and thinking through the transmission of signals from the brain to other parts of the body.
Physical Components of Nervous System	Human brains have approximately **100 billion neurons** (nerve cells). Each neuron contains a **cell body**, **axons** that **transmit** electrical impulses essential for signal transmission, and **dendrites** that **receive** these signals. Nerves are clusters of axons located across the body. **Glia** are non-neuron cells supporting nervous system function.
What are Neurotransmitters?	Messages are sent between neurons through **electrical signals** that become **chemical signals** at the end of an axon. This chemical signal is released through **neurotransmitters** into the synapse, the room from an axon's end to another neuron's dendrite tip. Most neurons will release the same neurotransmitter from their axons.
Types of Neurotransmitters	**Neurotransmitters** are either **small-molecule** transmitters or **neuropeptides**. Small-molecule transmitters will **act directly** onto nearby cells. Examples include dopamine and glutamate. Meanwhile, neuropeptides such as insulin or oxytocin work by **changing** how cells fundamentally **communicate at the synapse**.
What is the Endocrine System?	The **endocrine system** is a network of glands and organs, **regulating** various bodily functions through **hormones**. **Interactions** between hormones and the brain affect mood, behavior, growth, and cognition. Components are the pituitary, hypothalamus, pineal body, thyroid and parathyroid, thymus, adrenal, pancreas, ovary, and testis.

NIH (I), NIH (II), John Hopkins Medicine, Queensland Brain Institute, Dana Foundation

The Gut Microbiome Influence

The influence of the gut microbiome extends beyond the digestive system to the gut-brain axis and the immune, nervous, and endocrine systems. Companies seek to understand these connections better to create in-demand products.

Influence	Description
Gut-Brain Axis	• The gut-brain axis refers to the **two-way communication** between the gut and brain through the nervous system, endocrine system, and immune system regarding **diet and emotions**. • The global human microbiome market is rapidly growing with projections estimating **USD 4.9 billion by 2031**, growing at a **CAGR of 24.5%,** and top companies like **Axial Biotherapeutics** are looking to develop **microbiome-inspired therapeutics** for neurological disorders.
Immune System	• With **70-80% of immune cells** in the gut, the gut microbiota is closely related to the immune system. • Gut bacteria produce **metabolites** from dietary components, host products, or more, which the **innate immune system** uses to maintain intestinal mucosal lining and provide **non-specific defense**. • Commensal microbes **outcompete harmful microbes** for resource availability and niche opportunity. • **Pattern-recognition receptions (PRRs)** recognize specific microbe-associated molecular patterns (MAMPs) and **induce** chemokines and cytokines for **a protective immune response**.
Nervous & Endocrine System	• The **enteric nervous system (ENS)** is the part of the **automatic nervous system** that functions in the GI tract and controls digestion, and the **vagus nerve** is the main link between the ENS and the brain. • The gut microbiome influences **neuropod cells** that relay **mechanical, thermal, and chemical signals** within the gut as electrical pulses through afferent nerves on the vagus nerve to the brain. • Bacteria in the gut microbiome release neurotransmitters-like molecules **like serotonin** that travel through the endocrine system to the **blood-brain barrier** then into the brain.

Advances in Experimental Medicine and Biology, *Annals of Gastroenterology*, *Behavioural Brain Research*, *Gastroenterology*, *Nutrients*, *Scispot*

The Gut Microbiome and The Brain

The gut microbiome serves an important role in regulating the activity of neurotransmitters and hormones, communicating with the brain to influence overall health, including mental health conditions and neurological disorders.

Neurotransmitter Production

- The so-called "**second brain**" located in the walls of the digestive system is called the enteric nervous system (ENS) and made up of between **100** and **500 million nerve cells**.
- Gut bacteria in the digestive system **communicate** with the CNS by producing **neurotransmitters** like serotonin, GABA, and norepinephrine.
- Gut bacteria produce **short-fatty acids** (SCFAs) and **secondary bile acids** and metabolize **tryptophan** to aid in the process.

Gut-Brain Communication

- **Signals** from neurotransmitters and intermediate compounds like SCFAs **travel** to the brain through **afferent vagus nerve (VN) fibers** and are **returned** by the brain to cells in the gut wall and mucosal immune system through **efferent VN fibers**.
- These signals stimulate the VN fibers, **reducing inflammation**, and eventually lead to the **activation** of the **hypothalamic pituitary adrenal axis**. These processes **equilibrize** the gut microbiome.

Impact on Mental Health

- Research shows evidence of a **mind-gut link**.
- Between **30 and 40%** of patients with **depression** and **anxiety** have experienced **bowel issues** at some period.
- Certain **antidepressants** have been shown to be effective in **treating** symptoms of **irritable bowel syndrome**.
- Low levels of gut bacteria such as *Faecalibacterium* and *Bifidobacterium* have been connected to lower serotonin and GABA.
- One study found specific biological signatures in stress-resilient individuals.

Link to Neurological Disorders

- In **Parkinson's disease**, incorrectly folded alpha-synuclein proteins **migrate** from **gut enteroendocrine cells** to the **brain** through the VN.
- In **Alzheimer's disease**, research found amyloid-beta plaques are caused by **gut dysbiosis** from higher levels of *Bacteroidetes* and lower levels of bacteria in the *Firmicutes* families.
- In **multiple sclerosis**, researchers found that affected individuals have lowered levels of *Prevotella* and increased levels of *Akkermansia*.

Frontiers, NIH, NPR, Signal Transduction and Targeted Therapy, The Harvard Gazette

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Market Overview and Competitor Analysis

While stringent regulation makes market entry difficult, increased interest in gut health and precision medicine has consistently driven the growth of the global microbiome market, which encompasses a variety of application areas.

Global Human Microbiome Market Profile

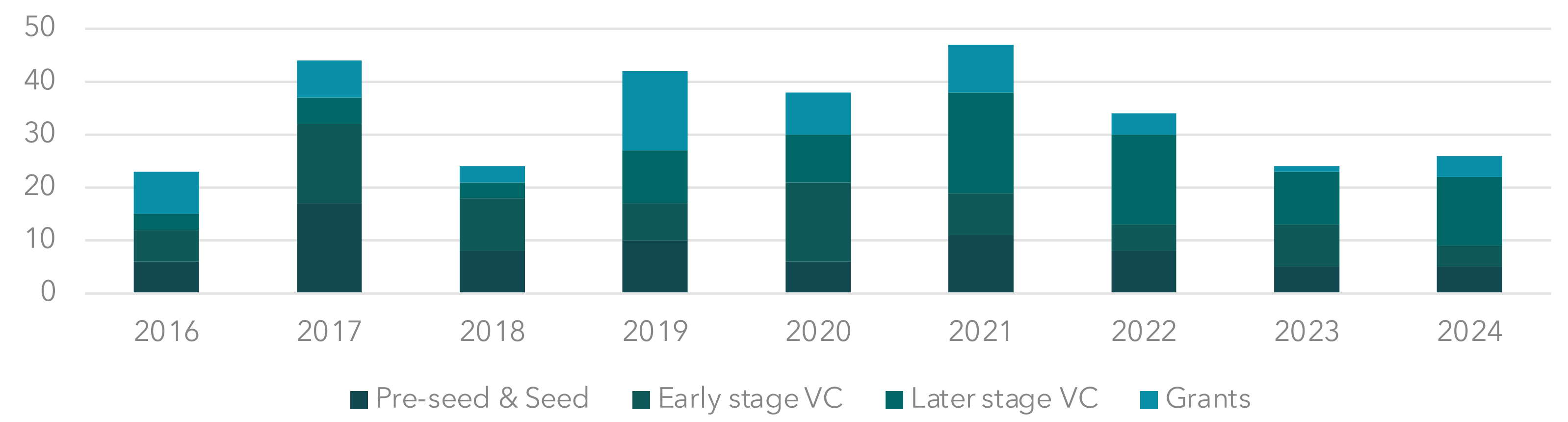
The global microbiome market is still in early stages of commercialization, with most products in clinical development, limited FDA-approved therapies, and increasing demand across digestive, metabolic, and immune-related conditions.

Microbiome Industry

- Investment and research have surged in the past decade, but **commercialization** is still **limited to a few FDA-approved therapeutics** and consumer supplements.
- Global microbiome market is **still emerging**, with most drug candidates in R&D or early-stage clinical trial phases.
- Estimated **valuation of the global microbiome market was USD 842M** in 2023.

MAJOR PLAYERS

SERES THERAPEUTICS
VEDANTA BIOSCIENCES
FERRING PHARMACEUTICALS
CJ BIOSCIENCE
SeedHealth



Regulatory Environment	Therapeutics are regulated as **biologics or drugs, requiring FDA premarket approval** (PMA) or investigational new drug (IND) applications. Many commercial microbiome products are currently classified as **supplements** which **bypasses FDA approval** but must still comply with **Dietary Supplement Health and Education Act (DHSEA)** and labeling regulations.
Market Drivers	**Growing interest in gut health, precision medicine**, and the gut-brain axis is driving demand for microbiome-based therapies. Another driver is **rising rates of IBD, obesity, and related chronic conditions**, which has pushed pharma companies to explore and invest in new therapeutics such as **symbiotics and live biotherapeutics (LBPs).**
Consumer Base	Primary consumers include **individuals managing digestive disorders** and younger **health-conscious individuals** seeking preventative supplements and DTC testing. There is also increased adoption among aging populations due to microbiome-linked immunosenescence. **Hospitals and clinics remain key buyers** of microbiome-based therapeutics.

FDA, Global Market Insights, Global Venturing, MarketsandMarkets, Modor Intelligence, Pitchbook, PWC

Human Microbiome Market Product Categorization

Products in the human microbiome market fall along a spectrum from highly regulated therapeutics to more general wellness tools, with each category differentiated by its clinical risk, regulatory path, target market, and intended use.

	Category	Details
Therapeutic Applications	Microbiome-Modulating Drugs	• Microbiome-modulating drugs, such as **FMTs and live biotherapeutic products (LBPs)**, aim to restore or modify gut microbial ecosystems to treat conditions like *C. difficile*, IBD, and **metabolic or neurological disorders**. Examples include Rebyota (FMT) and SER-109 (LBP), which both treat CDI. • Primary market is composed of **hospitals, clinical trial participants**, and patients with microbiome-disrupted diseases. Most products are **still in development** or clinical trial phases.
Therapeutic Applications	Microbiome-Derived Molecules	• These therapies **isolate or mimic microbial metabolites** to influence host physiology, targeting **immune** regulation or other **metabolic pathways**. For example, **Stellate Therapeutics**, is aiming to develop small microbial molecules to treat **age-related neurological disorders**. • These products are primarily in **preclinical stages**, attracting interest from biotech investors and pharmaceutical partners seeking **precision, non-live microbiome therapies**.
Commercial Applications	Functional Foods and Beverages	• Functional F&B are **modified food products that have additional health benefits** beyond its traditional nutrients. Examples include Olipop (prebiotic soda), De La Calle (probiotic soda), and The Coconut Cult (fermented coconut yogurt with specific multi-strain probiotics). • Main consumers are general **health-focused individuals**. Products are well-established and **widely available** in **grocery and wellness retail**, while market competition continues to drive innovation.
Commercial Applications	Consumer Biotics and Digital Health	• This segment includes **stand-alone probiotics, synbiotics, and pyschobiotics** (ex. Seed's DS-01, Bened Life's PS128) and data-driven **digital health platforms** like ZOE, which uses stool and blood tests to deliver personalized gut health and nutrition insights via app **direct to consumer**. • Primary market includes **health-conscious consumers** seeking personalized and proactive wellness tools. Products, typically categorized as supplements, are already **well-established on the market**.

Oroojzadeh (2022), Pitchbook

Market Overview and Competitor Analysis

While stringent regulation makes market entry difficult, increased interest in gut health and precision medicine has consistently driven the growth of the global microbiome market, which encompasses a variety of application areas.

Market Review: Microbial Therapeutics

The microbiome industry consists of many research areas, and the therapeutic or medical industry is expected to increase in global market shares, supported by an overall interest of researchers and pharmaceutical companies.

167 active compounds

There are **167 active compounds** of microbiome modulators and live organisms, ranking as the **top 15th mechanism** of action in current drugs on the research and development pipeline.

228.5 billion USD

The global market for healthcare-related microbial products was worth $147.4B in 2021 and $156.9B in 2022. It is projected to be worth more than **$228.5 B in 2027**, a **CAGR of 7.8%** over the next five years.

$100,000/year

Annual wages for microbiologists can range from **$40,000/year** to well over **$100,000/year** depending on **level of education** and **experience**.

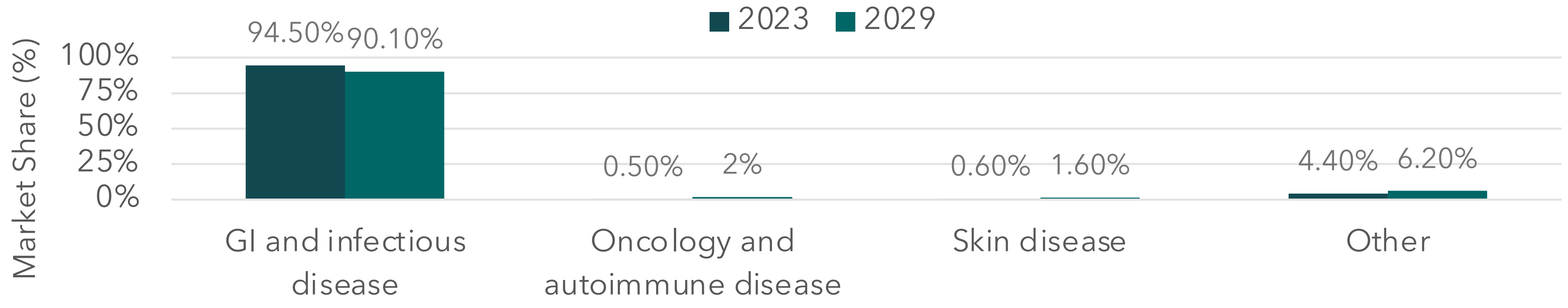
1.095 billion USD

Between fiscal years **2007 and 2016**, the NIH offered **$880 M worth** of funding to human microbiome research plus **$215 M for the HMP program**.

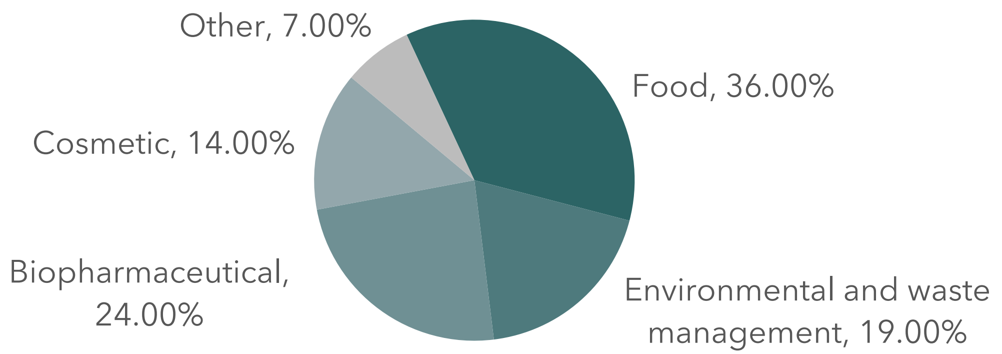
Key Takeaway

- Understanding the human microbiome is becoming **increasingly important** to the **pharmaceutical industry**.
- There is **substantial funding** available for active national projects and research dedicated to understanding the human microbiome.
- There is a **promising job market** for microbiologists, including **medical microbiologists** depending on qualifications.

Projected global human microbiome therapeutics market share, 2023 and 2029



Projected global industrial microbiology market share by application area, 2025



American Society for Microbiology, BCC, Microbiome, Statista (I), Statista (II), Statista (III)

Case Study: Seres Therapeutics

Seres is one of the most successful and influential microbial pharmaceutical companies in the United States, and they are most known for its development of the first FDA-approved oral microbiome therapeutic for *C diff.* called Vowst.

SERES THERAPEUTICS

- **Total Market Cap:** $124.92 M
- **Enterprise Value:** $186.56 M
- With a **1,672.2% increase**, Seres Therapeutics was listed as the **4th top** pharmaceutical and biotechnology company in **net sales growth**.
- **2nd top** company **by gain on the Nasdaq Biotech Index** in 2020 at **610.14%**.

MAJOR COLLABORATORS

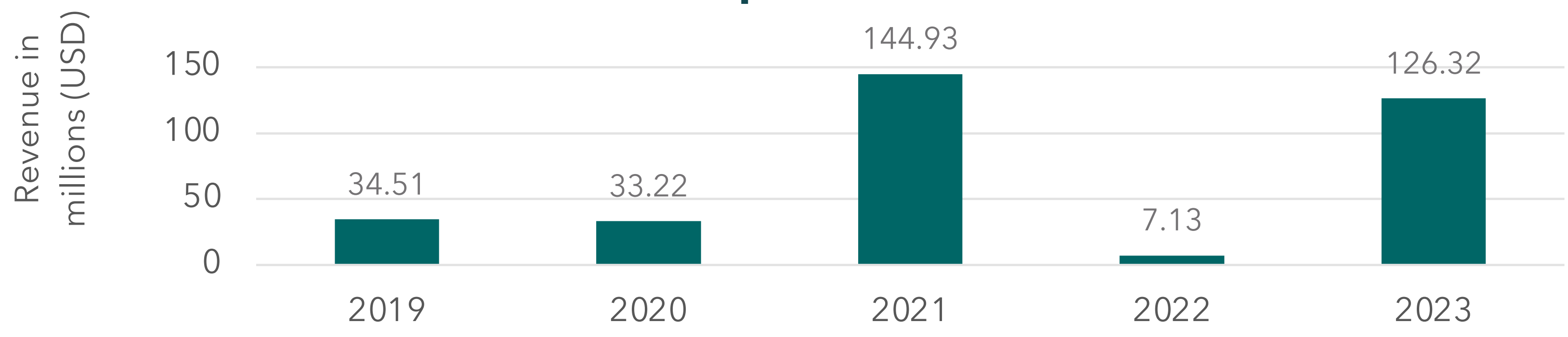
Nestlé HealthScience

CROHN'S & COLITIS FOUNDATION

Memorial Sloan Kettering Cancer Center

CARB-X Combating Antibiotic-Resistant Bacteria

Revenue of Seres Therapeutics from 2019 to 2023



Company History	• Founded in **2021**, Seres is now located in **Cambridge, MA** and incorporated in DE. • **Ser-109** (now **Vowst**) became the **first FDA-approved** oral microbiome therapeutic for preventing recurrent *Clostridioides difficile* infection **(CDI)** in adults in **2023**, and Seres was named a **"TIME100 Most Influential Companies"** for this achievement.
Products & Pipeline	• Seres Therapeutics is a **clinical stage** biotechnology company that specializes in using **live bacteria** to modulate the **composition** and **function** of the human microbiome. • The Seres **pipeline** is centered around **infections** and **immune modulation** therapies. • Seres' most notable product Vowst was sold to **Nestlé** in September of 2024.
Revenue Drop in 2022	• Seres' revenue 2022 can be explained by **a decrease in collaboration revenue**. • A 2021 License Agreement identified **Nestlé** as **lead commercialization party**. • Seres received an upfront license payment of **$175 million in July 2021** and an additional **$125 million in May 2023** following FDA approval of VOWST, but **none in 2022**.

EDGAR, Nestle, Quarterlytics, Seres (I), Seres (II), Seres (III), Seres (IV), Statista (I), Statista (II), Statista (III), Stock Analysis

Case Study: Finch Therapeutics

By leveraging its human-first discovery platform, clinical stage Finch Therapeutics has been pioneering microbiome therapeutics to try to solve currently unmet medical needs, although they have recently faced strategic adjustments.

Finch Therapeutics

- Founded in **2014** by Mark Smith and Zain Kassam.
- Finch Therapeutics is a **clinical stage** company, leveraging **clinical data** and **studies** to design microbiome-based therapeutics that target **dysbiosis**.
- Collaborations with leaders in the microbiome field like **Dr. Thomas Borody**, who established the Centre for Digestive Disease in Australia.
- Partnership with **Takeda** announced in 2019.
- Over **70** U.S. and foreign patents and over **140** patent applications that are awaiting approval.
- The company faces mixed reception after discontinuing the CP101 trial (thus decreasing its labor force by **95%**) despite positive Phase 2 Data.

> "Finch Therapeutics [was] formed to harness the **genomic revolution** and **machine learning** to pioneer **microbiome therapeutics**."

Portfolio's Mission

- Finch has designed a portfolio of products based on studies that suggest **microbiota** can be **transferred** from healthy people to those with disease.
- Company uses ***Human-First Discovery*** platform to develop **therapeutics** using microbiota from diverse human donors or those grown in pure culture.

Portfolio Highlights

- **CP101** is an orally ingested microbiome-based therapeutic for recurrent ***Clostridioides difficile*** infection (C. diff). Patent protected until **2036**.
- Pre-clinical microbiome-based therapeutics have also been designed to treat **ulcerative colitis**, **Crohn's disease**, and **autism spectrum disorder**.

Valuation and Growth

- As of recent updates, the company's valuation is not publicly disclosed.
- Finch is focused on realizing the value of its estate of **intellectual property** and other assets, after plans for CP101 Phase 3 trial were cancelled. It wants establish **additional funding/partnerships** to fund CP101.

Engaging Customer Base

- The company's target demographic is **patients** with **gastrointestinal diseases** (like C. diff) and **inflammatory conditions** (like ulcerative colitis).
- Engagement through **partnerships** with healthcare providers and clinical trial networks, emphasizing scientific efficacy and data-driven innovation.

Key Takeaway

Clinical-stage company Finch Therapeutics pioneers microbiome-based therapeutics, but has shifted focus after discontinuing its CP101 trials.

Finch Therapeutics (I), Finch Therapeutics (II), Finch Therapeutics (III), Global News Wire, Biospace, Microbiome Times

Market Overview and Competitor Analysis

While stringent regulation makes market entry difficult, increased interest in gut health and precision medicine has consistently driven the growth of the global microbiome market, which encompasses a variety of application areas.

Case Study: Microbiotica

Microbiotica has designed a leading platform to aid in the identification and isolation of gut bacteria for the development of microbiome-based therapeutics intended to target inflammatory diseases and cancer.

2016

In 2016, Microbiotica was founded in **Cambridge, UK**, using research from the **Wellcome Sanger Institute** to discover microbiome-based medicines and biomarkers.

2 LBTs

Microbiotica created two **live bacterial therapeutics** (LBT). **MB097** is intended for **cancer therapy**, improving immune checkpoint inhibitor's effects on cancer while **MB310** to treat **ulcerative colitis**.

£50M

In 2022, Microbiotica received £50 million worth of funding to advance their two LBT projects into **Phase 1b** of clinical trials. Additionally, other new discovery programs have advanced to the development stage.

MELODY-1

MELODY-1 is a **Phase 1b study** in the UK and EU to examine the effects of **MB097** for treating advanced **melanoma**. Phase1b also included Merck & Co.'s **KEYTRUDA** for when other therapies do not work.

COMPOSER

COMPOSER is a **Phase 1b study** to examine the effects of **MB310** when it is ingested once a day orally to treat those suffering with **ulcerative colitis**. The study is being conducted in the UK and EU.

5 Partners

Collaborations aid in clinical development and discovery research. Partners include MSD (Merck & Co., Inc.), the Crohn's & Colitis Foundation, Cancer Research UK, University of Adelaide, and Genentech.

Key Takeaway

- Founded by **Dr. Trevor Lawley** (of the Wellcome Sanger Institute) and **Mike Romanos**.
- In 2016, it created a leading platform for **identifying gut bacteria** from research about microbial culturing and its gut bacterial reference genome **database**. It uses the platform to examine the **microbiome profile** within patients, leveraging bioinformatics and machine learning processes.
- Mike Romanos said, "'[W]e are addressing the hurdles to translation by starting with clinic-based, precise determination of microbial signatures, using our uniquely accurate platform to identify microbes and mechanisms.'"

Microbiotica (I), Microbiotica (II), Microbiotica (III), Nature

Case Study: Viome

By leveraging its human-first discovery platform, clinical stage Finch Therapeutics has been pioneering microbiome therapeutics to try to solve currently unmet medical needs, although they have recently faced strategic adjustments.

VIOME LIFE SCIENCES **Viome**

- Founded in **2016** by Naveen Jain in Bellevue, Washington.
- Viome sells at-home **microbiome** health **tests** and then **personalizes nutrition** and **supplemental plans** based on results (utilizing **AI** technology). It is a well-established consumer wellness company,
- The company's products has been recognized by *Forbes*, *Men's Health*, *The Washington Street Journal*, and more.
- Viome's partners include Mayo Clinic, Mount Sanai, Macquarie University, UCLA, and Advent Health.
- Viome has a deal with **CVS** to sell at-home kits.

Formula for Precision Health

Biological Intelligence + Human Intelligence * Artificial Intelligence = Precision Health

Testing Model	• Customers can **subscribe** and receive an included **test** or start with just the test. Customers then **ship samples** from the test to a CLIA-certified **lab**. They complete a **survey** with questions to aid Viome in creating recommendations. Results return within **two weeks** with recommendations for Viome products.
Forms of Intelligence	• Viome utilizes a combination of **biological**, **human**, and **artificial intelligence** (their **Vi engine**) to make precise health recommendations. • Viome is also conducting various clinical studies with over 16,000 study enrollees across 20 chronic diseases (i..e. cancers, metabolic disorders, etc.)
Funding and Valuation	• Viome has exclusively licensed an **RNA analysis technology** that they claim is **1000 times** more efficient than other method for examining consumer samples. It performs tests for over **350,000** consumers across **106** countries. • In 2022, Viome was valued at **$339M** and secured **$175M+** in funding.
Products and Customer Base	• Viome sells products like **supplements**, "**gut formula**," **oral lozenges**, and **toothpaste**. Customers can purchase one-time test kits and then **subscribe** for ongoing supplement delivery and retesting. • Target health-wary consumers, emphasizing **empowerment** by **knowledge**.

Key Takeaway

Targeting health-conscious consumers through a subscription-based model and brand of empowerment, Viome provides at-home testing to customize recommendations for nutrition and supplements.

Viome (I), Viome (II), Tech Crunch

Market Overview and Competitor Analysis

While stringent regulation makes market entry difficult, increased interest in gut health and precision medicine has consistently driven the growth of the global microbiome market, which encompasses a variety of application areas.

Section 1: Market Overview

Section 2: Microbial Therapeutics Case Studies

Section 3: Discovery Platforms for Research Case Studies

Section 4: Consumer Health Case Studies

Case Study: Seed Health

Seed Health, leader in consumer probiotics, was founded in 2018 by Ara Katz and Raja Dhir and produces supplements for gut, skin, and overall health, utilizing engaging campaign strategies to target health-conscious individuals.

Discovery

- Seed Health utilizes a **human-first approach** across intellectual disciplines, including **computational biology**, to **examine** a host and their microbiome.
  - Pinpoint gut bacteria and their metabolites.
  - Search for **SNPs** to identify specific microbial genes.
  - Analyze microbes-host **interactions**.

Development

- Turn new revelations into therapeutics and products to be implemented in **real life** setting.
  - Examine and authenticate products with Chemistry, Manufacturing, and Controls.
  - **Streamline** user experience by strategizing, design, and implementing **user feedback**.

Clinical

- **Collect data** for product development from humans through **clinical trials**.
  - Formulate **standards** and methodology for conducting these clinical trials.
  - Utilize metagenomic, metatranscriptomic, and metabolomic **analysis** for both gut bacteria and host.
  - **Publish** findings.

Go-to-Market

- Transform inventive products into globally available **solutions** for **health** issues.
  - **Commercialization** through an omnichannel and **subscription-based** model and collaborating with **healthcare providers**.
  - Establish global **brand**.
  - Promote **environmental awareness** throughout supply chain process.

Current Products and Research

Seed Health produces two daily synbiotics **DS-01** (for adults) and **PDS-08** (for children) to ensure systemic bodily health. It also has developed **VS-01**, a synbiotic to optimize the vaginal microbiome. Additionally, the company is conducting **environmental research** through **SeedLabs**, under their "**One Health**" belief that human health and the environment are inextricably linked.

Seed Health (I), *Seed Health (II)*, *Seed Health (III)*, *Seed Health (IV)*

Case Study: Juno Bio

Juno Bio provides at-home testing to empower women to learn more about their vaginal microbiome and overall health; it has a vast number of online resources to engage its customer base.

1 Company Mission

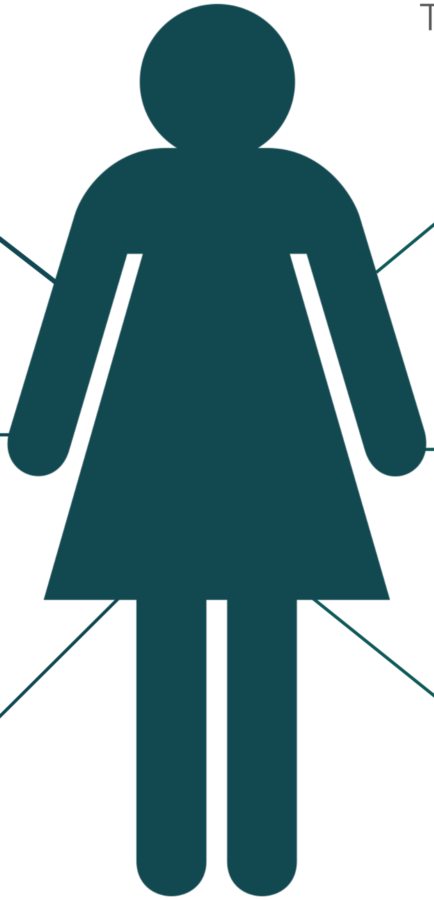
It aims to "**close** the **gender health gap**" by analyzing vaginal microbiome.

2 The Juno Study

It ran the largest study of its kind across **1000** U.S. **women** to power tests.

3 Juno Microbiome Test

At-home test using **sequencing** to analyze vaginal microbiome.



Blog 4

The company runs a **blog page** with advice about women's health.

Consumers 5

Juno Bio has worked with over **10,000** customers, with an overall rating of **4.8**.

Pricing Strategy 6

Offer tests **one-time** or **subscription**. Added value with various **perks**.

Key Facts

- Juno Bio was founded in **2018** by Hana Janebdar and Leighton Turner.
- Featured in *Vogue* and *Marie Curie*.
- The company has produced a **diagnostic test** that simultaneously analyzes an individual's vaginal microbiome and provides information for future research efforts.
- Managerial team includes **Gregory Buck**, who was the principal investigator of NIH's **Human Vaginal Microbiome Project**.
- Juno Bio fundraised **$251,000** with its largest investor being **Acequia**, a venture capitalist firm.

Global Venturing , Juno Bio (I), Juno Bio (II), Juno Bio (III)

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Emerging Opportunities for Commercialization

This section explores two rapidly growing areas of microbiome application, detailing both the current scope of scientific research and background knowledge as well as potential opportunities for expansion and market translation.

Section 1: Parkinson’s Disease

Section 2: Health Surveillance

Therapeutics for Parkinson's Disease: Overview

Parkinson's disease is a prevalent neurodegenerative disease that scientists are looking to better understand through microbiome research, where they hope to eventually create more effective biological treatments and/or cures.

Parkinson's Disease (PD)

Parkinson's disease is a **movement disorder in the nervous system**, and patients generally experience more and **increasingly severe** symptoms over time. Noticeable symptoms of PD include **tremors**, limb stiffness, trouble balancing, slowed muscle movement, slurred speech, and more. There is **no cure** for Parkinson's disease, but **treatments and surgery are available** options to mitigate symptoms.

Stakeholders

- The **risk of developing** Parkinson's disease **increases with age**, starting around **age 50**, and the average rate of onset of symptoms is around **70 years old**.
- **Males** are **1.5 times** more likely to develop Parkinson's disease than females.
- Approximately **25%** of Medicare Parkinson's disease patients are in **nursing homes**.

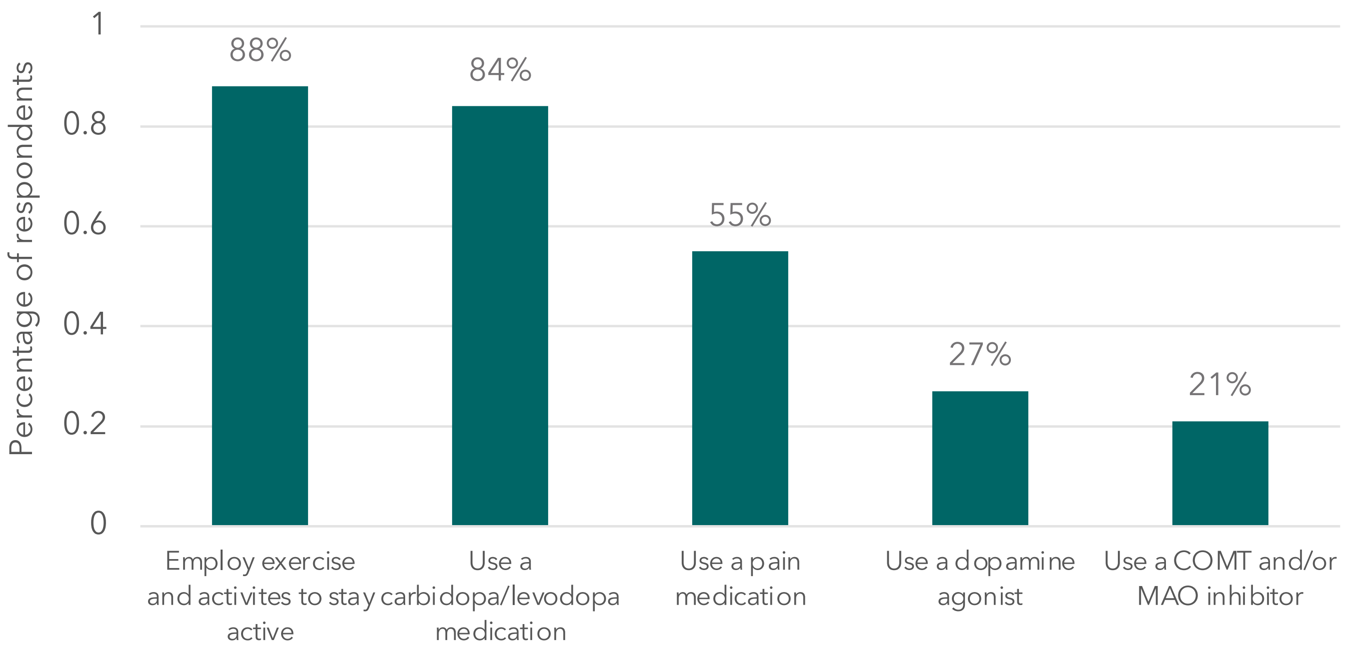
Market & Demand

- In the **United States**, around **1.8 M people** are projected to have Parkinson's disease **by 2030**, and each year more than **90,000 new patients** are diagnosed.
- It is also **the 2nd most common neurodegenerative condition** after Alzheimer's disease.
- PD is the **7th top therapy area** in the US **in 2022,** based on the number of prescriptions.

Existing Research

- As PD is **associated with GI conditions** like **constipation** and **stomach bloating**, experts are researching the possibility that the **gut microbiome** could be used as a **harbinger** or even identified as a **potential cause** of Parkinson's disease.
- Research shows that the **gut microbiomes** of **PD and non-PD patients** are **different**.

Self-Reported Use of Parkinson's Disease Treatments in the United States, 2019



Health Union , Mayo Clinic, Medical News Today, Neurology, Parkinsons.org, Pharmaceutical Executive

Therapeutics for Parkinson's Disease: Opportunities

Although still in its preliminary stages, Parkinson's disease appears to be connected to the gut microbiome, and it is one of the more well-researched areas of microbial influence in medicine, which will hopefully lead to microbiome therapies.

Science

Among non-movement symptoms, the early onset of **gastrointestinal dysfunction** is one of the most common.

Constipation is present in **70% of patients,** and **up to 75% of patients** will experience **speech or swallowing issues**.

Alpha-synuclein deposits in the brain cause PD symptoms, and alpha-synuclein has been **found along the GI tract** in PD patients.

Prevotella, *Faecalibacterium* and *Roseburia* are **reduced** in PD patients, but *Bifidobacterium* and *Lactobacillus* are **increased**.

Scientists hope that the **gut microbiome** may be a **precursor** to Parkinson's disease and offer an **entry point** for a **PD cure**.

Industry

As of October 2024, only **four published studies** on **fecal matter transplants** for PD exist, and only **one** is **formally registered**.

FMT studies were **placebo-controlled**, and subjects were diagnosed with PD for at most **7 years** (**mild to moderate symptoms**).

Only **eleven published studies** have looked at **probiotics**, and **all had positive** clinical outcomes on constipation and motor function.

Dietary changes and **prebiotics** allow for **selective enrichment** of certain microbial species, but **few studies** have applied this to **PD**.

Device-assisted therapies for PD can **alter** the gut microbiome, but **limited research** is available on the **reverse relationship**.

Frontiers, Neurotherapeutics, Parkinsons.org

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Microbiome-Based Health Surveillance: Overview

Lifestyle and dietary changes can interrupt the gut microbiome, increasing the risk for chronic neurogenerative and metabolic diseases; however, current diagnostic tools are invasive, costly, and not easily accessible to the public.

Rising Neurological and Mental Health Disorders

- Alzheimer's disease has deleterious effects on memory, thought, and overall cognitive function.
- **>50 million people** internationally have Alzheimer's disease, and this count is predicted to reach **131 million** in **2050**.
- Alzheimer's, other neurodegenerative, inflammatory, and metabolic diseases, are connected to the gut-brain axis.
- Further, **changes** in the gut microbiome and particular **biomarkers** have been linked to **young binge drinkers**.

Shifts in Environment and Lifestyle Choices of Patients

- **Westernized diet** can cause gut **dysbiosis**, as it interrupts the gut microbiome's balance and diversity.
  - Too much detrimental bacteria and too little helpful bacteria can affect various essential processes, leading to **disease**.
  - This is because the Westernized diet does not include enough **fiber** and **prebiotics** and is often composed of highly **processed** and **high-calorie** meals.

Limited Availability of Diagnostic and Early Detection Tools

- Current tools utilized to diagnose neurodegenerative diseases like Alzheimer's, such as PET scans or cerebrospinal fluid analysis, are quite **accurate** but **not** easily **accessible**, **costly**, and **invasive**. Therefore, they are not feasible in most healthcare settings.
- Therefore, there is a need for accurate, individualized tools to allow for timely and proper diagnosis of neurodegenerative diseases and thus optimal treatment.

Significance

Modern lifestyles and Westernized diets have driven microbiome alteration that can lead to the development of both cognitive and metabolic disorders, underscoring the need for non-invasive, accessible tools to track microbiome shifts and foresee risks to global health.

Drug Development and Delivery ,*NIH*, *NIH (II)*, *NIH (III)*, *NIH (IV)*

Microbiome-Based Health Surveillance: Opportunities

Technologies like wastewater epidemiology, wearable gut sensors, and predictive artificial intelligence models offer innovative, non-invasive, and scalable solutions for tracking the gut and overall health of a particular community.

Solutions for Monitoring Diseases Connected to the GBA

Existing Solutions

Wastewater epidemiology utilizes advanced molecular techniques to **track pathogens** (i.e. SARS-CoV-2) and **microbiome alterations** in sewage. Firms like **Biobot Analytics** use this approach for real-time, community-wide (local, regional, national) **detection** of **diseases**, to warn public health officials early.

Wearable gut sensors–such as AI-powered **ingestible capsules** and watches–offer **non-invasive monitoring** of GI activity, lifestyle, and metabolites. These technologies can **empower** patients to manage their gut health, perhaps improving early **detection** of **GI disorders** outside of clinics.

Emerging Concepts

Metabolites from the gut, such as short-chain fatty acid, Hippurate, and amino acids are found in urine, feces, and blood and can serve as **biomarkers for diseases** like IBD, Alzheimer's, and colorectal cancer. The products can be precisely examined to **enhance diagnosis** and **intervention**.

AI-driven predictive models utilized machine and deep learning to **examine** the gut microbiome and metabolome data. This information is used to **forecast** the **risk** for conditions such diabetes, IBD, and cardiovascular disorders. This tool offers **non-invasive**, **cost-effective** early identification.

Biobot , Frontiers, NIH (I), NIH (II), NIH (III), NIH (IV),, NIH (V), Penn State Health News , Research Features, Science Daily

Microbiome-Based Health Surveillance: Challenges

Microbiome surveillance has the potential for early disease prevention and intervention for chronic diseases, but requires interdisciplinary collaboration and transparency to address technical, social, and regulatory concerns.

Complex Data and Standardization

- There is a biological hurdle, presented by the fact that human **gut microbiomes vary** due to diverse diets, genetics, and environments. This therefore can **complicate** the process of **identifying** and **examining biomarkers**.
- As a result, scientists and researchers must develop **large**, **diverse datasets** and **synchronized protocols** for sampling and metagenomic analyses.

Public Trust and Ethical Risks

- As of 2023, **81%** of U.S. adults have **worries** about how firms use their data, and **71%** of U.S. adults have the same fears about the government. And most adults lack an understanding of what companies and the government even do with their data.
- Biometric data like microbiome profiles can **reveal sensitive information** about mental health risks or lifestyle that could lead to **insurance discrimination** risks.

Regulatory Standards and Monetization

- A monetary hurdle arises because there is a **lack** of **FDA** and **EMA guidelines** regarding microbiome-based public health tools (i.e. therapeutics vs. supplements). This gray area can therefore **delay investment** into microbiome-based startups.
- Therefore, these startups must undergo **high R&D costs** but lack a clear avenue by which to acquire **monetization**.

Drug Development and Delivery, *Pew Research*, *NIH (I)*, *NIH (II)*

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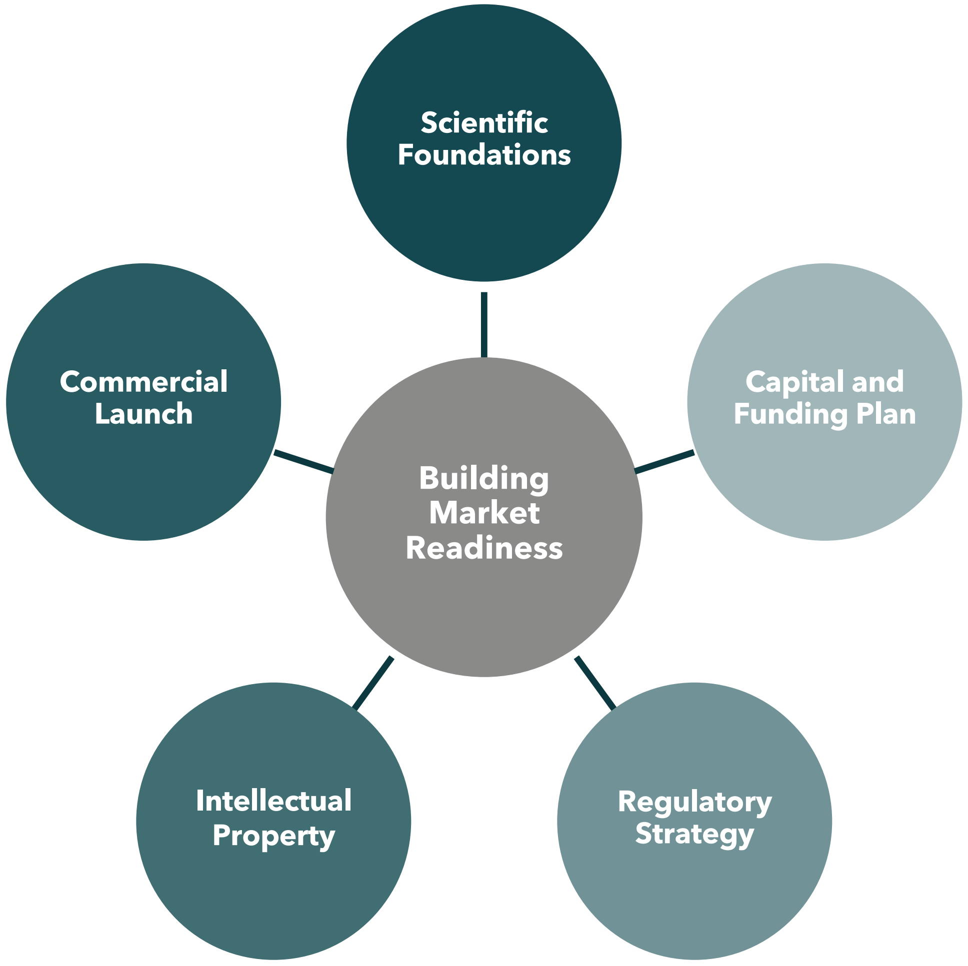
Key Strategic Considerations

This section summarizes strategic considerations for a startup attempting to enter the biomedical market . It also provides a development timeline which outlines the process of commercialization from pre-clinical research to market entry.

Key Strategic Levers for Biomedical Startups

Success in the biomedical space depends on startups' ability to demonstrate strong preclinical data, secure phased funding, obtain patents and regulatory approval, and build early commercialization plans to drive investor confidence.

Core Strategic Priorities



AdvaMed, Basel Area, Bio, BioCurate, Cytiva, FDA (I), NIH, Prisys Biotech

Actions & Considerations

1 – Scientific Foundations
~70% of drug development **failures** stem from **insufficient efficacy or toxicity** issues in **preclinical stages**. Biotech startups must demonstrate strong preclinical evidence, known as **proof-of-concept (PoC) to attract investors**.

2 – Capital and Funding Plan
Non-dilutive grants like NIH SBIR/STTR provide **up to $2 million** but **exclude business development** or marketing expenses. When moving toward clinical trials, start-ups typically **shift to VC to cover higher expenses** & operations.

3 – Regulatory Strategy
Companies must select the right FDA pathway based on product type and risk level. **Engaging FDA early** through pre-submission meetings can help validate regulatory approach and **reduce risk**.

4 – Intellectual Property
Filing a **provisional patent** early protects innovation and **permits refinement** before a **full utility application**. The **Patent Cooperation Treaty** (PCT) allows for a streamlined application process to **protect innovations internationally**.

5 – Commercial Launch
Only **~12% of drugs** entering trials receive **FDA approval**. Go-to-market plans should address **pricing, distribution, and payer strategy**. Licensing deals or pharma **partnerships** can **support scale** and accelerate access.

Strategic Partnerships in Microbiome Therapeutics

Analysis of two partnerships in the microbiome space reveals how long-term success is strongly tied to not only early funding and investor interest, but also clinical viability, broader market conditions, and sustained strategic alignment.

Takeda x FINCH

Takeda and Finch Therapeutics (2017-22)

- Partnership was established in 2017 when Takeda acquired **exclusive rights to Finch's oral ulcerative colitis candidate** FIN-524 for $10M upfront. Deal expanded in 2019 to include FIN-525 for Crohn's disease.
- The purpose of the partnership was to develop microbiome-based therapeutics, identified through **Finch's Human-First Discovery platform**, to modulate **immune responses in IBDs**.
- **Takeda invested over $44M** through upfront, milestone, and R&D reimbursement payments, which supported Finch through **early-stage R&D and clinical development**, helping advance key candidates toward the IND and Phase I stages.
- This partnership drew **early optimism** as a sign of **pharma's growing interest in microbiome** therapeutics.
- Collaboration **ended in 2022** when Takeda exited several microbiome programs following broader setbacks in the field, leading **Finch** to **pause clinical trials** and **cut ~95% of its staff** to preserve capital.

Nestlé HealthScience x SERES THERAPEUTICS

Nestlé Health Science and Seres Therapeutics (2016–)

- Partnership was established in 2016 to co-develop and commercialize microbiome therapeutics, **providing Seres with $120M upfront**.
- In 2021, deal expanded to **co-commercialize SER-109 (Vowst)** in the U.S. and Canada. Seres provided $175M upfront, with a $125M milestone payment upon FDA approval, and agreed to **share profits equally**. Nestlé was involved in **commercial launch strategy**, such as physician education and marketing.
- Seres received **strong positive press** as a **milestone** for microbiome drug commercialization and as **validation of Seres' platform**.
- In Sept 2024, Seres finalized the **sale of all rights to Vowst** to Nestlé, but they will provide **transition services** and continue to share in profits until the end of 2025. Seres is also **eligible for future milestone payments**.
- Post-sale, Seres is now focusing on **advancing other microbiome therapeutics** in their pipeline, most notably SER-155.

BioPharma Dive, BioSpace, Finch (I), Finch (II), Nature Reviews Drug Discovery, Nestle (I), Nestle (II), Seres (I), Seres (II), Takeda

Differences in Regional Regulatory Environments

Regional regulatory differences shape the speed and strategy of market entry, making it essential for biotech startups to understand approval pathways and identify opportunities for streamlined expansion, scaling, and strategic partnerships.

EMEA: European Union

The **European Medicines Agency (EMA)** offers a **centralized procedure**, which allows for **single-market authorization** across EU member states and Iceland, Liechtenstein, and Norway. This pathway is **required for innovative medicines** such as biologics and orphan drugs. Other options such as the **decentralized procedure and Mutual Recognition** allow companies to **expand approval** country by country.

EMEA: UK and South Africa

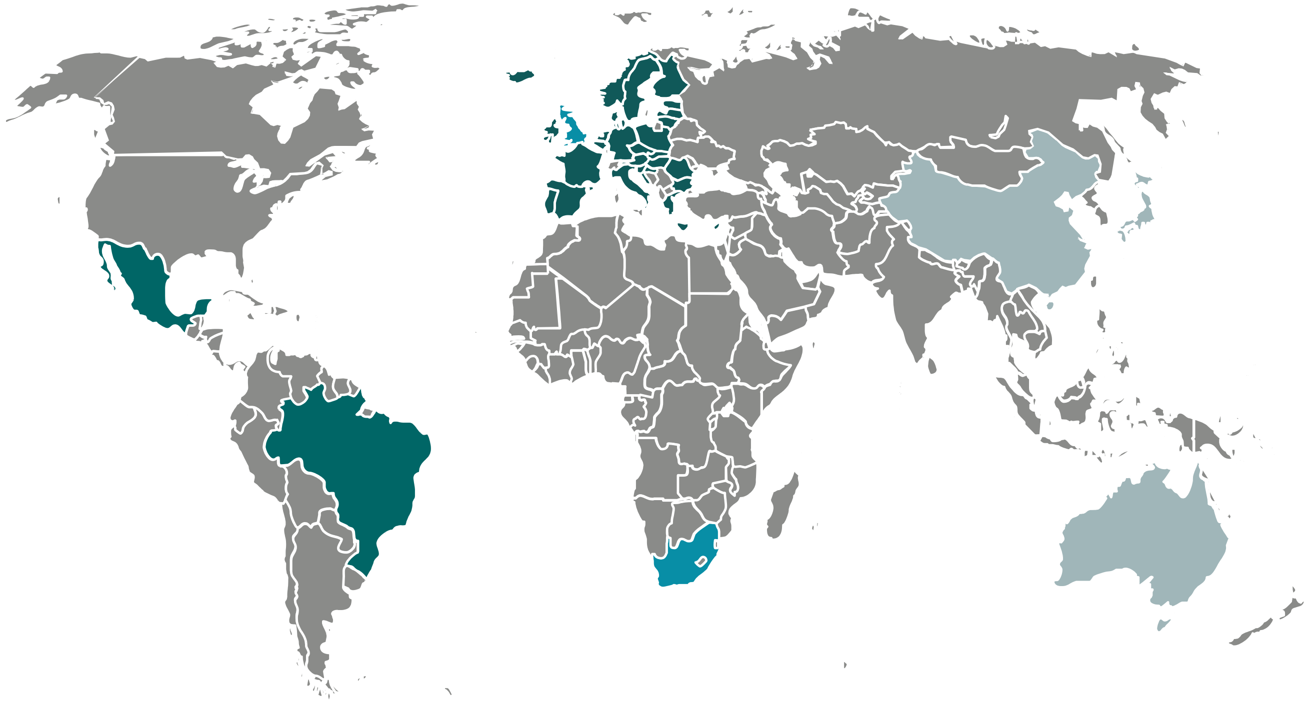
In the UK, the **Medicines and Healthcare products Regulatory Agency** (MHRA) oversees approvals, offering fast-tracked approvals through **Innovative Licensing and Access Pathway** (ILAP). **South Africa's** SAHPRA is more under-resourced but is working to speed up drug approvals through the **ZaZiBoNa initiative** – a regional effort to **streamline medicine approvals across SADC** countries.

APAC: China, Japan, and Australia

Japan's Pharmaceuticals and Medical Devices Agency (PMDA) and **China's** National Medical Products Administration (NMPA) offer a **priority review track** for innovative drugs. **China** accepts some **foreign trial data**, while **Japan** typically **requires local trial data**. **Australia's** Therapeutic Goods Administration (TGA) supports **quick approvals** through Provisional and Priority Review often **without regional trial data**.

LATAM: Mexico and Brazil

Brazil does **not offer a faster approval** process **for innovative drugs**. **Mexico's** regulatory body, **COFEPRIS**, has signed agreements allowing **recognition of approvals from EMA and FDA** in some product categories, facilitating faster entry. Though LATAM is not as developed of a market, both countries are **attracting increased investment for early-stage trials** and sustainable **health innovation**.



Role of the International Council of Harmonization (ICH)

- Reduces duplication in clinical trials and submissions through **harmonized technical guidelines** such as Good Clinical Practice **(GCP), stability, and nonclinical safety**.
- Helps startups **streamline approvals in multiple regions** by encouraging global trial design and documentation consistency.
- Includes **23 members** with voting rights, and **38 observers**, who can participate in discussions and adopt guidelines voluntarily.

ANVISA, EMA, Global Regulatory Partners, ICH, SAHPRA, TGA, UK Gov, Zazibona

End-to-End Development Timeline for Biomedical Startups

The development and commercialization timeline for biomedical ventures can span 10+ years, with each phase from pre-clinical research to product launch requiring coordinated strategy and early preparation for long-term success.

Pre-Clinical

Duration: 2-3 years
Estimated Cost: Varies widely, $15-100M
Key Actions:

- Collaborate with **academic institutions** or **contract research organizations (CROs)** to conduct toxicology and pharmacology studies.
- Generate **PoC data** through lab (in vitro) and animal (in vivo) studies to **evaluate safety and efficacy**.
- Consider filing **provisional patent** to **protect early innovations** ahead of full patent applications.

Clinical Research

Duration: 6-7 years
Estimated Cost:

- Phase I: $1-2M
- Phase II: $7-20M
- Phase III: $20-100M+

Key Actions:

- *Phase I*: **20–80** healthy volunteers or patients to **test safety.**
- *Phase II:* **~100–300** patients to assess **efficacy and side effects**.
- *Phase III:* **300–3,000+** patients, confirming **effectiveness** and monitoring **adverse events**.
- Trials must align with **good clinical practice (GCP)** standards to ensure **data integrity**.

FDA Approval

Duration: ~10 months for standard application review
Application Fee: Varies from **~$20K-4M+** based on application type

- Other costs include consulting, on-site visit, and registration fees.

Common Types:

- *IND*: **Required to begin human trials** for drugs and biologics.
- *510(k):* For **moderate-risk devices**; must prove **substantial equivalence** to a predicate.
- *NDA:* Required to market a **new small-molecule drug**; must include clinical, safety, & manufacturing data.

Market Entry

Duration: Preparation starts **~18-24 months** before target launch date.
Estimated Cost: Varies based on promotional, sales, and other overhead business expenses.
Key Actions:

- Begin **go-to-market planning** during **late clinical trials.**
- Launch targeted **marketing campaigns** and initiate dialogues with **key opinion leaders (KOLs), healthcare providers, and payers** to build engagement.
- Ensure promotional materials adhere to **regulatory standards**.

Ongoing Growth

Duration: Often evaluated in **1-3 year phases** post-launch.
Key Actions:

- Potential **Phase IV clinical trial** to monitor long-term safety & efficacy.
- **Analyze and collect real-world evidence** (RWE) to evaluate performance, support payer negotiations, and identify new patient segments.
- Explore **public and private exit strategies:** M&A, IPO, PE, and Special Purpose Acquisition Companies (SPAC) mergers.

Biolife Solutions, FDA (I), FDA (II), FDA (III), Greenfield Chemical, Progress in Medical Sciences Journal, UC College of Medicine

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Expert Interviews

By conducting eleven interviews with experts and professors across immunology, neuroscience, drug discovery, and entrepreneurship, the team gained key insights into the current state of research and translational challenges.

Section 1: Medical Experts

Section 2: Industry Experts

Interview: PI at Brigham and Women's Hospital (BWH)

An interview with a PI at BWH discussed how gut-trained immune cells, which drive CNS diseases, can be targeted by probiotics and outlined critical considerations for translating gut-brain axis research into viable therapeutic products.

Gut-Brain Axis Mechanisms

- This expert conceptualizes the gut-brain axis in three major ways: **immune cells migrating** from the gut **to the CNS**, gut-derived **metabolites** influencing CNS cells, and direct **nerve connections**.
- His research focuses on CNS diseases like **multiple sclerosis (MS) and glioblastoma**, as well as IBD.
- His lab is developing **engineered probiotics** that aim to **prevent** immune cell **migration** or **limit inflammation** in the CNS.

> "**Immune cells** that cause **tissue destruction in the CNS** are trained and activated in the **gut**. This opens up **new opportunities** in therapeutic interventions because it suggests that you can **target the gut to control brain diseases**."

Key Translational Considerations

- This expert believes successful translation requires finding a **balance** between **regulatory** strategy, **scientific efficacy**, strong **intellectual property** (IP) **protection**, and **investor appeal**.
- **Securing capital** to move promising candidates into clinical trials is a **major challenge**, especially given the **current funding landscape**.
- He also sees **company creation** as a necessary **precursor** to **translating research** into therapeutics.

> "We need to find that **sweet spot** between having **IP**, having an **effective**, therapeutic **intervention**, and having something that is **palatable for investors** to result in **company creation** and then develop new **therapies**."

Interview: PI at Harvard Medical School (HMS)

An interview with a PI at HMS discussed how microbiota influences immune system development, as well as expectations for future therapeutic strategies that leverage microbial molecules to modulate specific host–microbe interactions.

Microbiome & Immunology

Germ-free mice have **underdeveloped immune systems** and the **distribution of cells** found in their lymphatic system is **different from colonized mice**. His lab demonstrated that the microbiome influences the immune system through **molecular interactions**.

"By just giving the [germ-free] mouse pure PSA… you could balance the TH1 and TH2 cells the way that a whole microbiota does."

Mechanistic Blind Spots

Initially, many microbiome **studies aimed to** enumerate, identify, and **classify all the microbes** of a particular species or those present in different diseases. In the 2010s, **hundreds of microbiome companies** were founded, but this expert believes most went **bankrupt** due to **mechanistic failures**.

"And the reason they went bankrupt is that they had an observation, but they didn't understand the mechanisms."

Therapeutic Future

This expert expects future microbiome-based therapies to rely on identifying and **modifying individual microbial molecules**. These molecules could be **used directly or mimicked** through medicinal chemistry to precisely **target host systems**.

"I think the future of microbiome research is molecular. It's identifying which molecules are involved in these specific interactions."

Interview: Principal Investigator at Beth Israel

An interview with a PI at Beth Israel highlighted current questions the gut-brain axis field aims to answer and how limited mechanistic understanding of gut-brain signaling has stalled therapeutic progress, despite growing commercial interest.

> "We went through this **whole hype cycle** where people started associating microbiota, microbiome with everything. However, the complexity of the field is so immense. What exactly is the **nature of that microbiota interaction**, and how is it **important in a clinical setting**, is something that we don't clearly understand. And it is an area that **requires extremely important mechanistic studies** to be done."

Current Field Focus	▪ A key focus in the field is identifying **which neurons in the brain communicate with which neurons in the gut** and decoding the **molecular language** they use. Researchers are also investigating **innervation of the gut**, aiming to clarify **how signals move in both directions** across the GBA and determine which gut functions the brain controls and vice-versa.
Translational Gaps	▪ Despite significant investment, the **microbiota field has produced few tangible therapies**. Most **consumer-facing products** like probiotics and prebiotics are sold as **supplements**, not FDA-approved medications, meaning their efficacy remains scientifically unverified. Fecal microbiota transplants **(FMTs) for recurrent *C. difficile* infections** are the **only approved intervention**.
Existing Therapies	▪ Some **existing medications already act on GBA circuits**, though not explicitly marketed as thus. **Ozempic**, a GLP-1 agonist, affects GBA functions like **satiety and gut motility**. Some nausea medications like **Zofran blocks 5-HT3 receptors** in the gut and CNS. **Gepants**, a form of **migraine medication** target receptors found in **GBA circuits without entering the brain**.

Interview: PI & Professor of Immunology at HMS

This interviewee is an expert in neuroimmunology. Their lab has shown that sensory neurons can directly sense bacterial mediators and neurotransmitters, and they have also studied how bacteria can invade the meninges and the brain.

> "The most **innovative things** I think really come from **basic research labs** just trying out different things. And the **big breakthroughs** like if we were to treat autism or pain, I think some **revolutionary idea** would come from some **chance observations** often."

Industry Evolution	This expert describes that the **neuroimmunology** field has "really exploded" over the past few years, especially in the context of **multiple sclerosis**. They say that neuroimmunology has caught that attention of experts in industries from neurology to immunology who are interested in the **intersection**.
Gut Brain Axis	In addition to the previously discussed interactions along the gut-brain axis, this expert points out that changes in the **stimulation of pain fibers** in the gut can also influence the gut microbiome and potentially be used to help **maintain a healthy composition** of the gut microbiome.
Future Timeline	This expert believes that the biggest **scientific breakthroughs** happen in **lucky accidents** in **research labs**. Additionally, this expert suggests that in addition to a lack of understanding of the gut microbiome, there also yet to exists a **complete map of all neurons** in the gut.

Interview: PI at Channing Div. of Network Medicine (CDNM)*

An interview with a PI at CDNM revealed new trends in the therapeutic space and explored how computational modeling techniques and machine learning are being leveraged to predict microbiome behavior and identify drug candidates.

> "We are very interested in **the interspecies interactions and assembly rules** of [the microbiome]. So, we are developing **deep learning** methods to understand how species interact and to **predict the metabolic profile and metabolite response** to **different perturbations**, such as particular dietary interventions, aiming for **precision nutrition**."

Predictive Modeling Approach	▪ The lab uses **neural ordinary differential equations (neural ODEs)** to model microbiome dynamics by mapping the relationship between a **binary vector** (indicating **microbial community membership**) and a **vector** representing the **relative abundances of those species**. This enables the model to predict **species abundances** based on differing presence or absence patterns.
Promising Therapeutics	▪ An important development in microbiome therapeutics is the move toward **well-defined bacterial cocktails**, like **Vedanta's 8-strain consortium for CDI** (now in clinical trials). Unlike donor-derived FMTs, these products are standardized. **Autologous FMTs** are also being explored for **stem-cell transplant patients**, for whom **restoring one's own microbiome** post-treatment may aid recovery.
AI-Driven Discovery Tools	▪ Many of the lab's computational tools are adapted from computer science, such as **long short-term memory (LSTM)** models and **convolutional neural networks (CNNs)**, which are used to identify **antimicrobial peptides (AMPs)** in the urinary microbiome that may inhibit pathogens like E. coli and serve as **antibiotic alternatives**. This approach is paired with **in vitro validation**.

**CNDM is affiliated with Harvard Medical School (HMS) and Brigham and Women's Hospital (BWH)*

Interview Insights: Neurogastroenterologist

A neurogastroeneterologist who actively practices medicine and conducts clinical research says that new technologies allow scientists to better establish causal relationships between the microbiome and neurological conditions.

Causation

For **ethical** and **logistical** reasons, it is **difficult** to experiment with **human** microbiomes and thus **unable to establish causal** relationships.

*"One of the **fundamental problems** with microbiome research... the microbiome is **extremely varied** in the millions fold type of variation, it is easy to find an **association** between many different types of conditions and changes in the microbiome… They're **not causations**, and that is a key **fundamental difference**"*

Non-Invasive Methods

Advancements in the neurogastroenterology field use **non-invasive technologies** like encapsulated **sensor pills**, **radioactive** pineapple pudding MRI techniques, and **fMRI** to measure neurological and gut health.

*"A common state of **evolution**, with regards to the GI tract and the enteric nervous system are different evolutions of **techniques** to measure how stuff moves in the GI tract, from **invasive to less invasive**"*

Opinion

This physician personally does **not** think the microbiome is the **sole cause** of all GI diseases but sees the value of it in treating GI conditions.

"As we get more sophisticated in understanding by either **human experiences** or **animal model** conditions, what specific groups or classes of microbiota could be the culprits or the consequences of changes... we can be much **more precise** about how we **modulate these negative populations of microbiome**"

Interview: Postdoctoral Research Fellow at CDNM

An interview with a research fellow at CDNM emphasized the challenges of translating microbiome research from animal models to humans and pointed to a future driven by personalized microbiome solutions and multi-strain therapeutics.

Translational Challenges

- The human **microbiome is highly mutable**, and dietary changes, daily exposures to new microbes, a course of antibiotics, etc. can all influence its composition.
- Unlike animal models, humans live in **uncontrolled environments**, making it **difficult to translate findings**.
- Due to the sheer number of microbes and **complexity of microbial interactions**, therapeutic solutions which only consider **one strain may not be functional**.

"We have trillions of microbes in our bodies. It's **not a simple question** of looking at **one specific strain** of microbes. We have to consider **all the direct and indirect interactions** between those microbes."

Future Directions

- There is **high microbiome variability across individuals** which makes **one-size-fits-all** therapeutic approaches **unlikely to be successful**.
- This researcher believes **personalized microbiome** applications are **currently neglected** but will become a larger focus in the future.
- He also expects future approaches to focus on **microbial consortia** (groups of bacteria that work together).

"**Everyone has a different baseline**. If you discover a microbiome that might increase happiness, then make a pill based on that microbe—it won't necessarily work. I believe the **future** will be more **focused on personalized medicine**."

Interview: Professor at HMS and BWH

An interview with a professor at Harvard Medical School and Brigham and Women's Hospital discussed market and startup strategies, specifically regarding the process of commercializing biotechnological discoveries.

On the Transition from Academic Research to Product Development

"[T]here's **no formula**… Every technology, **every company** is **different** and it's different because of not just the particular focus of the company, but because of the people… I always come back to [the fact] that you have to **make sure** that you get the **right people** involved… [I]n order to be successful in the commercial sector, just like anything, you need to **gain experience**… [I]f you think that just because you discovered something as a **scientist**… that you can be the **CEO** of that company… you have a lot… to learn."

Are There Signs That a Product Has Start-Up Potential?

"You have to make sure… that whatever your discovery is, **there is a market** for it… You'd have to make sure that there's **no** pre-existing **intellectual property**… [Y]ou might think you have a great idea… go into the **patent literature** [and] find out that somebody thought about it 20 years ago, and… started a company [that] failed… [T]he other question is… is this a **standalone discovery**… or something that just would make somebody else's product better?... [**S**]**tarting** a **company** vs. **licensing** the **technology**… [is] a big decision."

Expert Interviews

By conducting eleven interviews with experts and professors across immunology, neuroscience, drug discovery, and entrepreneurship, the team gained key insights into the current state of research and translational challenges.

Section 1: Medical Experts

Section 2: Industry Experts

Interview: Researcher and Pharmaceutical Co-Founder

This expert has extensive experience in drug research and has helped co-found many pharmaceutical companies, helping to provide scientific support. Their lab focuses specifically on drug delivery systems and tissues creation.

Industry Evolution

The drug delivery field has evolved over the past few years to move **ideas** to **proof of principle** experiments in **animal models** like the Moderna mRNA vaccine and growing human tissues on chips.

Pharma Start-Ups

Based on this expert's background in company start-ups, they describe an **idea starting in a lab**, then receiving a **patent** for the design, then **building the company** around the patent and the scientific methodologies.

Microbiome Companies

This expert notices that there have been several start-up microbiome-based companies that **haven't done well** within the larger pharmaceutical industry because so much about the microbiome has **yet to be understood**.

Interview: Senior Lecturer at Harvard Business School (HBS)

An interview with a senior lecturer at HBS outlined key considerations for translating academic research into startups, highlighted early-stage funding strategies in life sciences, and emphasized the importance of early regulatory planning.

Translating Research

- This expert believes successful translation begins with **identifying valuable IP and securing strong patents** early.
- Academic spinouts should decide whether **researchers** will **build the venture** themselves **or license technology** to external firms.
- Ventures should also consider the **state of the market** and **how applicable** their product is.

"First of all, identify what is the intellectual property that you're creating – what's unique about it. Is it just science for the sake of science, or is there a practical application?"

Funding and Growth

- Most **early-stage** biotech ventures rely on a mix of **seed funding**, **government grants** (ex. SBIR, NIST), and other **non-dilutive financing** for initial R&D efforts.
- **Startups** turn more to **VCs** after **PoC** is established and **regulatory pathways** become **clearer**.
- Funding needs also **depends on** the **type of product** (i.e. medical devices vs. biologics).

"There's no hard and fast rule, but most companies use a combination of early funding and non-dilutive financing to get to a point where the technology is validated."

Regulatory Strategy

- He advises **frequent** and **early communication** with the FDA or other regulatory bodies to help shape development strategies.
- **Global regulatory** planning should begin early to **maximize acquisition** or **commercialization** potential.
- In LS entrepreneurship, **product-market fit** must be **validated early** as regulatory commitments make **late pivots very difficult**.

"Once you're in a regulatory framework, you can't really experiment a lot, you can't pivot, or you can't change very often."

Interview: Founding Dir. of a Bioengineering Research Institute

An interview with this founding director emphasized the importance of technical de-risking and strong leadership teams in biotech success and discussed the funding constraints facing early-stage ventures and microbiome commercialization.

> "When you do a startup, you have to focus, focus, focus. You're **no longer doing research**; you're doing **technology development for a specific application**, with investors who are thinking purely from a financial perspective. You have to deal with things like **manufacturing, scale up, regulatory, freedom to operate, intellectual property,** and **raising money** all the time."

Venture De-Risking	▪ Early technical de-risking is critical for startups. **De-risking** includes proving **reproducibility**, **validating results** through **external studies**, and addressing **manufacturing** and **regulatory risks**. Additionally, building a strong **patent portfolio** and ensuring **freedom to operate** are essential steps for ventures to **attract investors** and position themselves for commercialization.
Successful Teams	▪ This expert emphasized that while VCs are interested in the technology/product being developed, they **primarily fund teams** of people who **function well together** and are **passionate, focused and capable**. Early-stage founders should demonstrate **leadership** experience, operational readiness, as well as the ability to **work synergistically under** financial and technical **pressure**.
Funding Challenges	▪ Early-stage biotech companies often rely on **seed funding, grants, and foundation support**, but **aligning funding sources with long-term business goals** is crucial. This expert noted that **investor enthusiasm** is difficult to predict and is currently at **a low point** for the biotech sector. He also warned that **cuts to university endowments** will further **constrain venture funding**.

State of the Field: Summary of Expert Interviews

Experts noted that while the gut-brain axis is linked to many diseases, establishing causality remains a major challenge, and future therapeutic progress will likely focus more on personalized solutions and engineering microbial molecules.

Current Understanding

- The GBA has been **implicated in many diseases** such as MS, Alzheimer's, autism, ALS, and mental health disorders, though it's **difficult to determine causation**.
- Current **research** focuses on uncovering specific **molecular mechanisms** and **functional pathways** rather than microbiome numbering and composition studies.
- Some existing drugs, like **Ozempic** and **pain and nausea medications**, already **act on gut-brain circuits**, though they were not specifically designed to do so.

Translational Barriers

- There is **significant microbiome variability** between individuals, which makes it **more difficult** to develop standardized and **broadly effective therapeutics**.
- Changes to the **scientific funding landscape** and **limited investor interest** in the biotech space create major hurdles for translating microbiome-based research.
- Many experts discussed how **establishing causality** between **specific microbes and disease outcomes** is **difficult**, which slows translation and therapeutic development.

Future Expectations

- Some experts anticipate that future therapies will likely **target individual microbial molecules** or engineered **biological pathways** rather than whole microbiota.
- **Personalized microbiome** solutions, such as tailored **microbial consortia** and engineered **non-engrafting probiotics**, are gaining traction among researchers.
- **Computational modeling** and **AI drug discovery techniques** are increasingly being used to **predict microbiome behavior** and identify **therapeutic targets**.