



# BIOMICA

# Microbiome-Empowered Therapeutics

Dr. Elran Haber, CEO • June 2023

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# We are Biomica

A clinical-stage biopharmaceutical company with cutting edge computational capabilities to develop the most optimized microbiome-based therapeutics.





### Rooted in excellence

Subsidiary of Evogene Ltd. (NASDAQ, TASE: EVGN), a pioneer in the field of applied computational predictive biology, creating next-generation life sciences products.



#### Breakthrough platform

Drug candidates identified and designed with PRISM – a proprietary computational platform combining AI capabilities with big data.



#### Spearheading the future

Optimized discovery, design & development, resulting in best-inclass pharmaceuticals.

Precise & efficient – from concept to clinical trials in only 3 years.



# **Our Mission**

To discover & develop novel therapies for microbiome-related human disorders.

We utilize computational predictive biology to provide new therapeutic modalities for high-value, unmet medical needs. Showing promise in immune-mediated & infectious diseases

Current programs:



Immuno-oncology



Gastrointestinal (GI) related disorders



Antimicrobial resistance (AMR)

# Harnessing the human microbiome



microbes in the human body



Trillions of microorganisms live in & on our bodies



Play an essential role in various daily bodily functions



Microbiome diversity is associated with health & wellbeing



## **Right field**, **right time**



### **Key Players**

#### **Big pharma**







#### **Active companies**



MiEVELO

SERES

### Most candidates are still in the discovery & preclinical stages; Increasing number advancing to clinical stage

- GI-related disorders (44%)
- Cancer & Immunemediated Diseases (35%)

#### Sources:

BCC Research (2017) -Human Microbiome-based Drugs and Diagnostics Market SVB – Emerging Healthcare: Microbiome Investment Trends Aug 2017)

https://www.microbiometimes.com /the-microbiome-biotechlandscape-an-analysis-of-thepharmaceutical-pipeline/

### Right field, right time

# The microbiome is flourishing

**STAT+** 26 April, 2023

FDA approves Seres microbiome drug, as field advances

In Vivo 🍌

Informa Pharma

Intelligence

17 June, 2021

### The Microbiome's Time To Shine

Exclusive Interview With Seventure CEO Isabelle de Cremoux

26 January, 2021

The century of the microbiome: an exciting time for human health

PHARMACEUTICAL TECHNOLOGY 2 July, 2021 Seres and Nestlé enter up to \$525m deal for microbiome therapeutic

### A clinical promise comes true

MicrobiomeTimes Nov 9, 2022

BiomeBank announces regulatory approval for donor derived microbiome drug

Pharmaceutical Technology Dec 1, 2022

ical US FDA approves Ferring's Rebyota for Clostridioides difficile infection

Pharmaceutical Technology Apr 27, 2023 Seres and Nestlé Health receive FDA approval for Vowst microbiome therapy

First Microbiome drugs approved by FDA & more positive clinical data shows strong validation of microbiome therapeutics

# Limitations of common approaches

	Number of microbial entities	QC	Scalability	Druggability	Patentability	COGS	Targeted multiple functions composition	Potency*	Safety**
Fecal Microbiota Transplantation (FMT)	_	_	_	$\checkmark$	$\checkmark$	$\checkmark$	_	$\checkmark$	$\checkmark$
Single-strain method	~~	~~	~~	~~	$\checkmark$	~~	_	$\checkmark$	~~
Multi-strain rationally- designed Live biotherapeutic products (LBPs)	$\checkmark$	~~	$\checkmark$	~~	~~	_	~	<b>~ ~</b>	$\checkmark$



# Finding the optimal combination of microbes is complex

To develop **best-in-class drugs**, one must find, select, and combine **only the most suitable microbes** from the thousands of strains in our bodies.

### Each method has its own set of challenges





## Computational, targeted & function-based drug design





Modulating a patient's microbiome Computational predictive biology platform Function-based drug design process





# Proven, robust data integration, analysis & prediction



tens of millions of

dollars invested

of experience

Validation through collaborations with industrial leaders & internal results



2

Computational predictive biology platform



# Holistically determining the best strains for the patient

Patients' microbiome: Identifies the strains present & the functions they perform



Strain identifier

Function finder

Strain-function allocator

Computational predictive biology platform

2

Patients' genetic & clinical data: Examining the patient's clinical data & genomic data

Clinical data

🛣 Human 🚆 genomics

🚡 Consolidator

Analysis, integration & prioritization Computational & researcherguided selection of candidate microbes

Drug





Function based drug design process

# An emphasis on microbial function

PRISM allows high resolution analysis to rationally design therapeutics **based on microbial functions\***.

This differentiates Biomica from current practices.



#### \* Functions:

Genetic elements (e.g. genes, operons, pathway, plasmids) and/or their biosynthetic products (e.g. metabolites, proteins, enzymes)

# The optimal combination

Up to 4 bacterial strains are carefullyselected, based on their functions, which may work across several complementary mechanisms.



Minimum no. of microbial strains

Maximum relevant & complementary functions



### **Optimal therapeutic impact**

# Biomica's optimal therapeutic outcome

	Number of microbial entities	QC	Scalability	Druggability	Patentability	COGS	Targeted multiple functions composition	Potency*	Safety**
Fecal Microbiota Transplantation (FMT)	_	_	_	$\checkmark$	$\checkmark$	$\checkmark$	_	$\checkmark$	$\checkmark$
Single-strain method	~~	~~	~~	~~	$\checkmark$	~~	_	$\checkmark$	~~
Multi-strain rationally- designed LBPs	$\checkmark$	~~	$\checkmark$	~~	<b>~~</b>		$\checkmark$	~~	$\checkmark$
Biomica's rationally- designed LBPs	~~	~~	~~	~~	~~	~~	~~	~~	~~



# The pipeline

	Program	Indication / Target	Discovery	Preclinical	Phase 1 / POC	Phase 2	Approach
Immuno- oncology	BMC128	Combination Therapy with ICI* for Solid Tumors					<b>B</b>
GI-related	ВМСЗЗЗ	IBD					<b>®</b> ,
disorders	BMC426	IBS					<b>®</b> ,
Antimicrobial	BMC202	C. difficile Infection					E
(AMR)	TBD**	MRSA Infection					E

\* Immune checkpoint inhibitors

16

\*\*Biomica in collaboration with Nobel Prize Laureate Prof. Ada Yonath at Weizmann Institute of Science to develop a selective treatment for MRSA infection.

🛞 Live biotherapeutics

Small-molecule

Response to immunotherapy through specific bacterial functions



# **POC in humans**

Modulating gut microbiome improves cancer treatment

### Science

NEWS | HEALTH

# Fecal transplants could help patients on cancer immunotherapy drugs

Early results hint that benefits seen in mice could extend to people

5 APR 2019 · BY JOCELYN KAISER

www.sciencemag.org/news/2019/04/fecal-transplants-couldhelp-patients-cancer-immunotherapy-drugs ...Now, another potential therapy is being tested in clinical studies: fecal transplants. Early results from two groups described at the annual meeting of the American Association for Cancer Research (AACR) here this week suggest some patients who initially did not benefit from immunotherapy drugs saw their tumors stop growing or even shrink after receiving a stool sample from patients for whom the drugs worked...

...One unresolved question is exactly which microbes help ramp up the desired immune activity...

## **POC in humans**

Modulating gut microbiome improves cancer treatment

### Science

Reports

Cite as: E. N. Baruch et al., Science 10.1126/science.abb5920 (2020).

### Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients

Erez N. Baruch<sup>1,2\*†</sup>, Ilan Youngster<sup>3,4</sup>, Guy Ben-Betzalel<sup>1</sup>, Rona Ortenberg<sup>1</sup>, Adi Lahat<sup>5</sup>, Lior Katz<sup>6</sup>, Katerina Adler<sup>7</sup>, Daniela Dick-Necula<sup>8</sup>, Stephen Raskin<sup>4,9</sup>, Naamah Bloch<sup>10</sup>, Daniil Rotin<sup>8</sup>, Liat Anafi<sup>8</sup>, Camila Avivi<sup>8</sup>, Jenny Melnichenko<sup>1</sup>, Yael Steinberg-Silman<sup>1</sup>, Ronac Mantani<sup>11</sup>, Hagit Harati<sup>1</sup>, Nethanel Asher<sup>1</sup>, Ronnie Shapira-Frommer<sup>1</sup>, Tal Brosh-Nissimov<sup>12</sup>, Yael Eshet<sup>4,8,13</sup>, Shira Ben-Simon<sup>10</sup>, Oren Ziv<sup>10</sup>, Md Abdul Wadud Khan<sup>14</sup>, Moran Amitt<sup>13</sup>, Nadim J. Ajami<sup>14</sup>, Iris Barshack<sup>4,8</sup>, Jacob Schachter<sup>1,4</sup>, Jennifer A. Wargo<sup>14,16</sup>, Omry Koren<sup>10</sup>, Gal Markel<sup>1,2,17</sup><sup>9</sup><sup>‡</sup>, Ben Boursi<sup>4,18,19</sup><sup>‡</sup>

### Science

Clinical Trials

Davar et al., Science **371**, 595–602 (2021) 5 February 2021

## Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients

Diwakar Davar<sup>1</sup>\*, Amiran K. Dzutsev<sup>2</sup>\*, John A. McCulloch<sup>2</sup>, Richard R. Rodrigues<sup>2,3</sup>, Joe-Marc Chauvin<sup>1</sup>, Robert M. Morrison<sup>1</sup>, Richelle N. Deblasio<sup>1</sup>, Carmine Menna<sup>1</sup>, Quanquan Ding<sup>1</sup>, Ornella Pagliano<sup>1</sup>, Bochra Zidi<sup>1</sup>, Shuowen Zhang<sup>1</sup>†, Jonathan H. Badger<sup>2</sup>, Marie Vetizou<sup>2</sup>, Alicia M. Cole<sup>2</sup>, Miriam R. Fernandes<sup>2</sup>, Stephanie Prescott<sup>2</sup>, Raquel G. F. Costa<sup>2</sup>, Ascharya K. Balaji<sup>2</sup>,

www.science.org/doi/10.1126/science.abb5920

www.science.org/doi/10.1126/science.abf3363





# **Combination therapy**

Initial focus on solid tumors: Lung cancer (NSCLC), renal cell carcinoma (RCC), and **melanoma**. Biomica aims to **improve clinical response** to ICI through immunomodulating combination therapy.





Next gen. optimized consortia A new combination providing the selected microbial functions & presenting higher likelihood for survival in GI.

## BMC128 administered prior to and in combination with anti-PD1 significantly improved anti-tumor activity



\* BMC 128 - Comprised of 4 live bacterial strains derived from BMC121 and BMC127

### BMC128 demonstrating efficacy against melanoma

### BMC128 significantly enhanced anti-tumor activity, resulting in an increased response of melanoma tumors to anti-PD1

BMC-128 Anti-PD1





CISION PR Newswire

13 April, 2021

#### Biomica Announces Positive Pre-Clinical Results, Demonstrating Efficacy of BMC128 in Melanoma

USA - English 🗸

Biomica's live biotherapeutic drug candidate, BMC128, significantly increased anti-tumor activity in combination with Immune Checkpoint Inhibitors in Melanoma. First-in-human, proof of concept study expected later this year



These results demonstrate the potential applicability of BMC128 and its relevance to treating multiple types of solid tumors.

# Advancing into the clinical phase



BMC128 consists of **4 live bacterial strains**.



Results demonstrated a significant **reduction of tumor volume**, and **increased animal survival** compared to anti-PD1 therapy alone.



**MoA is immune mediated** – Increased tumor inflammation & infiltration of T lymphocytes and NK cells.



Potential applicability in the treatment **various types of solid tumors**.

CISION<sup>®</sup> PR Newswire

11 July, 2022

Biomica Announces Successful Enrollment of First Patient in its Phase I Study of Microbiome-Based Immuno-Oncology Drug USA-English





# POC first-in-human

### First Patient dosed July 2022

A phase 1, open-label study to evaluate the safety and tolerability of **BMC128** in combination with anti-PD-1 (Opdivo<sup>™</sup>) in patients with **non-small cell lung cancer** (NSCLC), **melanoma** or **renal cell carcinoma** (RCC), <u>who</u> progress on immunotherapy



### ,H1 2023

preliminary results and first data points readout expected in early 2023



expected to be enrolled in this phase I trial.



of the BMC128 and anti PD-1 combination will be investigated as primary objective.



### **Exploratory objectives**

are to explore efficacy variables in response to combined treatment with BMC128 and anti PD-1.



### **BMC128 FIH Study design**



<sup>25</sup> DLT, Dose-limiting toxicity; EOT, end of treatment; EOS, end of study

\* https://clinicaltrials.gov/ct2/show/NCT05354102?term=bmc128&draw=2&rank=1



IBS & IBD



# Irritable bowel syndrome (IBS)\*

A common intestinal functional disorder, group of symptoms: Abdominal pain, constipation or diarrhea, bloating, gas & diarrhea.



### Inflammatory bowel disease (IBD)

A group of inflammatory conditions of the colon and small intestine (Crohn's disease, ulcerative colitis & pouchitis).



\*In collaboration with The University of North Carolina (UNC) at Chapel Hill

### Both clearly related to the microbiome

Biomica pushes the barriers posed by existing therapies by addressing the **underlying cause of the disorder, rather than the symptoms**.

https://www.grandviewresearch.com/industryanalysis/irritable-bowel-syndrome-ibs-treatment-market

https://www.grandviewresearch.com/industryanalysis/inflammatory-bowel-disease-ibd-treatment-market **IBS (40M)** IBS-D (16M) IBS-C (14M) IBS-M (9M)

IBD (3M)

Pouchitis (150K)

IBS (\$1.5Bn)

IBD (\$19.2Bn)

Crohn's disease (2M) Ulcerative colitis (1M) 43M Patients Est.

**20.7Bn** USD

### Established role for microbiome in IBD etiology

A state of inflammation is associated with reduced richness of microbial taxa and functions

> Gastroenterology. 2017 Feb;152(2):327-339.e4. doi: 10.1053/j.gastro.2016.10.012. Epub 2016 Oct 18.

Roles for Intestinal Bacteria, Viruses, and Fungi in Pathogenesis of Inflammatory Bowel Diseases and Therapeutic Approaches

#### R Balfour Sartor <sup>1</sup>, Gary D Wu <sup>2</sup>

#### Affiliations

- <sup>1</sup> Departments of Medicine, Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina. Electronic address: rbs@med.unc.edu.
- 2 Division of Gastroenterology, Perelman School of Medicine, the University of Pennsylvania, Philadelphia, Pennsylvania. Electronic address: gdwu@mail.med.upenn.edu.

PMID: 27769810 PMCID: PMC5511756 DOI: 10.1053/j.gastro.2016.10.012

**BMC333** 

Optimized drug candidate derived from Biomica's drug candidates BMC321 and BMC322

Aimed to reduce inflammation for treating IBD

> Curr Treat Options Gastroenterol. 2015 Mar;13(1):105-20. doi: 10.1007/s11938-014-0042-7.

#### Therapeutic Manipulation of the Microbiome in IBD: Current Results and Future Approaches

#### Jonathan J Hansen <sup>1</sup>, R Balfour Sartor

#### Affiliation

<sup>1</sup> Department of Medicine, University of North Carolina at Chapel Hill, CB 7032, Chapel Hill, NC, 27599, USA, jjhansen@med.unc.edu.

PMID: 25595930 PMCID: PMC4364996 DOI: 10.1007/s11938-014-0042-7



Drug comprised of 4 bacterial strains, detected through Biomica's proprietary computational functional genomic analysis platform.



Strains selected for their anti-inflammatory functions, complement each other and target both immunocytes and intestinal mucosal cells.



Each strain supports growth and metabolism of other strains, along with favorable gut resident bacteria.





### BMC333 reduces inflammation and tissue damage









### BMC333 reduces inflammation and tissue damage



MC333 consists of **4 live bacterial strains**.

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Results demonstrated a significant **reduction of inflammation**, and **intestinal tissue damage** in several in vivo models.



**MoA is immune mediated** – involving induction of IL-10, increased regulatory T cells and B cells in Iamina propria and systemic.



Potential applicability in the treatment of IBD.

#### CISION<sup>®</sup> PR Newswire

13 April, 2022

Biomica Announces Agreement with Sheba Medical Center for Joint Microbiome Clinical Research USA-English-

The research will be focused on developing new treatments for Inflammatory Bowel Disease (IBD)







# Antimicrobial resistance (AMR)

Targeting multi-drug resistant bacterium while preserving healthy gut microbiome

### C. difficile infection (CDI)

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525ED
- 00 -

Most common hospital-acquired infections (Over 600,000 a year).



Increasing cause of morbidity and mortality.



Developing a selective anti-bacterial agent designed to inhibit the C. difficile toxin.

### **MRSA** infection

A collaboration between Biomica and the Nobel Prize Laureate Prof. Ada Yonath at the Weizmann Institute of Science.

In-licensed IP and knowhow generated by Prof. Ada Yonath.

Cause to tens of thousands of annual cases of mortality in the US.



Due mostly to hospitalization, the economic cost of CDI (est.)





# Upcoming advancements

### Predictions for patients' response to ICI

# The potential for future drugs



# **\$20M Funding Round**

### December 2022





Led by **Shanghai Healthcare Capital (SHC)**, a leading Chinese private equity fund, focused on biotech and healthcare investments

# An experienced management team



#### Elran Haber, PhD, MBA CEO

Previously served as the CEO of Therapix Biosciences (Nasdag, TASE: TRPX), leading the company to a successful IPO on Nasdag and advancing the Company's programs to clinical stage. Spent more than 10 years as Chairman and board member of several privately held. and publicly traded companies. Served in senior executive roles in various life science companies and a private investment firm. Holds a PhD in Pharmaceutical Science and an MBA in Finance & Financial Engineering, both from The Hebrew University of Jerusalem, Israel.



#### Prof. Yehuda Ringel CSO

Chief of the Gastroenterology and Hepatology Division of the Meir Medical Center in Israel; Professor of Medicine at Chapel Hill, North Carolina and is affiliated with University of North Carolina Hospitals.

Has more than 30 years of diverse experiences, especially in Gastroenterology and translational research, and is an expert on IBS and functional motility disorders; Recipient of several prestigious awards. MD from Technion Institute of Technology, Israel.



#### Shiri Meshner, PhD **VP of Research & Development**

Previously served as the head & principal investigator of the Dead Sea microbiology lab in the Dead Sea-Arava Science Center.

Spent over 5 years working in the pharma industry both in the US and in Israel (OSI pharmaceuticals and Teva pharmaceuticals). Holds a PhD in systems microbiology from the Department of Physics of Complex Systems at The Weizmann Institute.

#### **Yifat Zommer VP Finance**

Prior to joining Biomica, served as a finance advisor to public and private companies. Prior to that, she served as Chief Financial Officer of Oramed Pharmaceuticals Inc. (NASDAQ, TASE: ORMP) from 2009 to 2017. Holds a Bachelor of Accounting and Economics degree from the Hebrew University, an MBA from Tel-Aviv University and a Masters degree in Law (LL.M.) from Bar-Ilan University, Israel, and is a certified public accountant.

## **Board of** directors



#### **Ofer Haviv** Chairman

Mr. Ofer Haviv serves as Evogene's (Nasdag: EVGN) President and CEO since of late 2004.

#### Jing Bao, MD, PhD Director

Dr. Bao is a partner of Shanghai Healthcare Capital, has with more than 30 years of experience in cancer research, infectious disease control, fund management and drug clinical trials

#### **Doron Ben Ami** Director

Mr. Doron Ben Ami is a highly experienced executive with a successful track record of more than 20 years of in the Pharma industry.



#### Kinneret Savitsky, PhD Director

Dr. Kinneret Livnat-Savitzky is a Managing Partner in Team8 Health. Previously served as the CEO and board member of FutuRx Ltd (OrbiMed, J&J Innovation and Takeda's accelerator), with over 25 years of experience in the biopharmaceutical industry.











## World-class scientific advisory board & advisors



#### Prof. Yehuda Ringel

Chief Division of Gastroenterology and Hepatology at Meir Medical Center, Israel. Professor of Medicine at Chapel Hill, North Carolina and is affiliated with University of North Carolina Hospitals.



#### Prof. Willem M De Vos

Professor and Chair of Microbiology at Wageningen University, the Netherlands and Professor of Human Microbiomics at the University of Helsinki, Finland.



#### Prof. R. Balfour Sartor

Serves as the Midget Distinguished Professor of Medicine, Microbiology and Immunology and Director of the Multidisciplinary IBD Center at the University of North Carolina, Chapel Hill.

#### **Prof. James Versalovic**

Pathologist-In-Chief at Texas Children's Hospital and Director of Texas Children's Microbiome Center, Professor and Vice Chair of Pathology & Immunology at Baylor College of Medicine.



#### Prof. Gal Markel

Director of the Davidoff Cancer Center & Deputy Director General of the Rabin Medical Center. An internationally recognized expert in translational tumor immunology and clinical immunooncology.



#### Prof. David Rubin

Section chief of gastroenterology, hepatology, and nutrition at University of Chicago Medicine. Chair-elect of the National Scientific Advisory Committee of the Crohn's and Colitis Foundation.



#### Dr. Ravid Straussman

Principle investigator of the Tumor microenvironment, tumor microbiome and resistance to anti-cancer therapy lab at the Weizmann Institute of Science, Israel.

## Summary



Human microbiome-based therapeutics is a rapidly growing space, and represents a multi \$Bn market opportunity.



Biomica develops innovative microbiome-based therapeutics utilizing dedicated computational predictive biology tools.



Biomica's computational tools and unique approach provide a significant differentiation.



Clinical POC preliminary results and first data point readout expected in early 2023



Focus on high-value clinical programs for the development of therapies for antibiotic resistant bacteria, immunooncology and microbiome-related gastrointestinal (GI) disorders.



Experienced management team, board of directors & world-class scientific advisory board.



# Thank you!

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