

Global Engage 


**7<sup>TH</sup> GLOBAL MASLD**  
CONGRESS

**LONDON**  
24-25 JUNE 2024

**7<sup>TH</sup> GLOBAL MASLD**  
CONGRESS



**Dr. Juan Basterra**  
CEO

 **Mikrobiomik**  
rethinking microbiome

 25 June, 2024

 London, Uk



The background of the slide is a microscopic image of numerous green, rod-shaped bacteria, likely Bacillus subtilis, arranged in various orientations and overlapping each other. The bacteria are semi-transparent, showing internal structures like flagella and spores. The overall color palette is a monochromatic green.

**1. Mikrobiomik in a nutshell**

**2. MASH & FSPIM**

**3. EMOTION phase II clinical trial**

**4. LIVERGUT phase III clinical trial**

**5. Take a home message**

The background of the slide features a dense field of blue, rod-shaped bacteria, likely representing the microbiome. The bacteria are rendered with a semi-transparent, 3D effect, showing their individual shapes and orientations. They are scattered across the entire frame, creating a textured, biological backdrop for the text.

**1. Mikrobiomik in a nutshell**

**2. MASH & FSPIM**

**3. EMOTION phase II clinical trial**

**4. LIVERGUT phase III clinical trial**

**5. Take a home message**





Where do  
we come  
from?

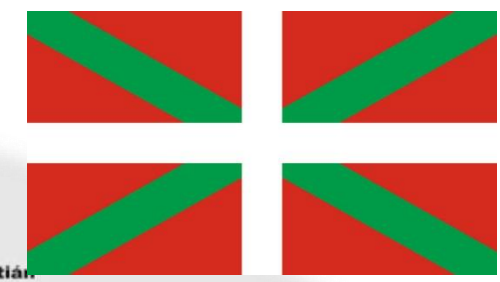
180°W 150°W 120°W 90°W 60°W 30°W 0° 30°E 60°E 90°E 120°E 150°E 180°E



**CENTER OF THE WORLD**

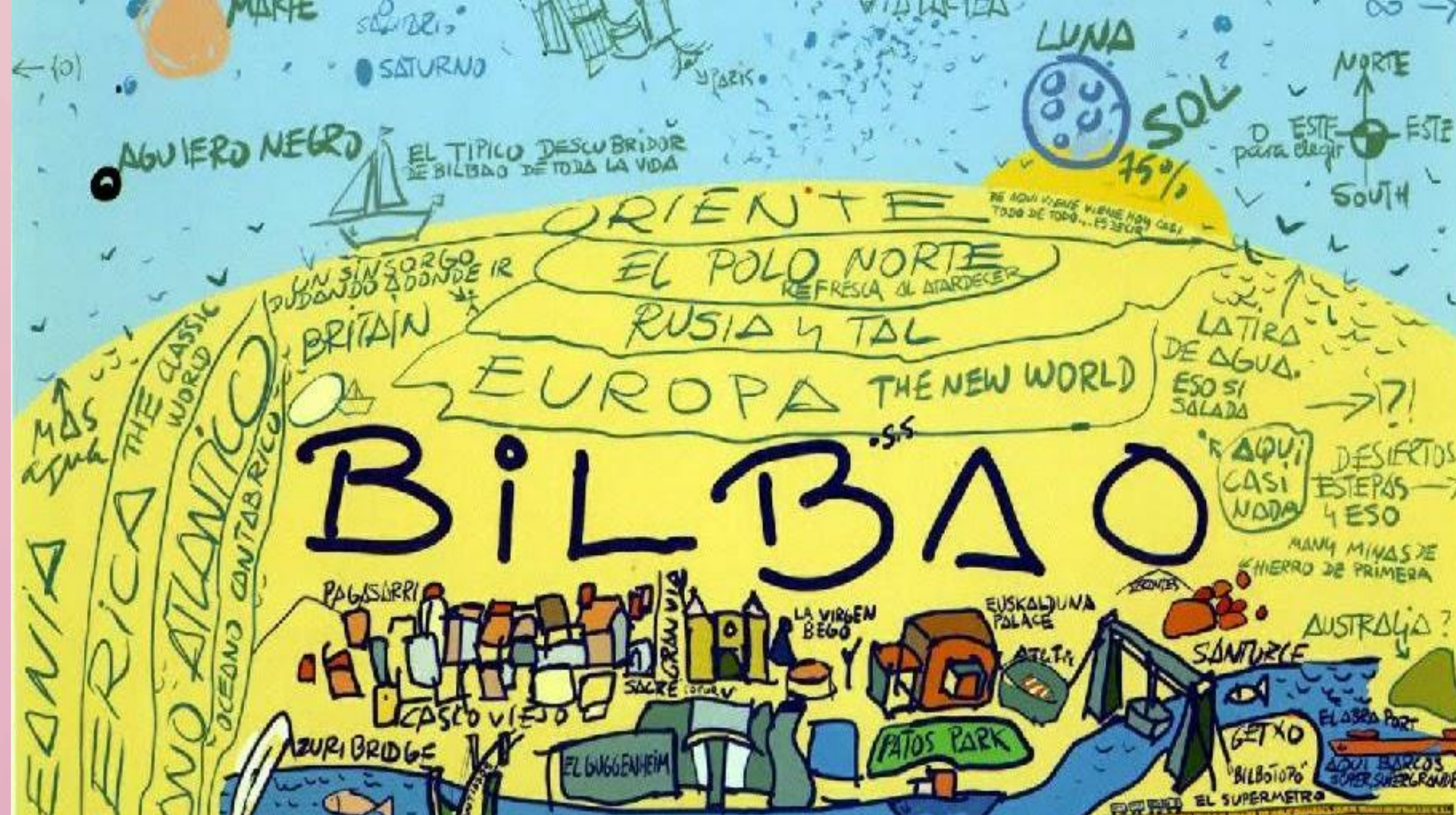


# Basque Country





# Bilbao







# MATRIARCHY

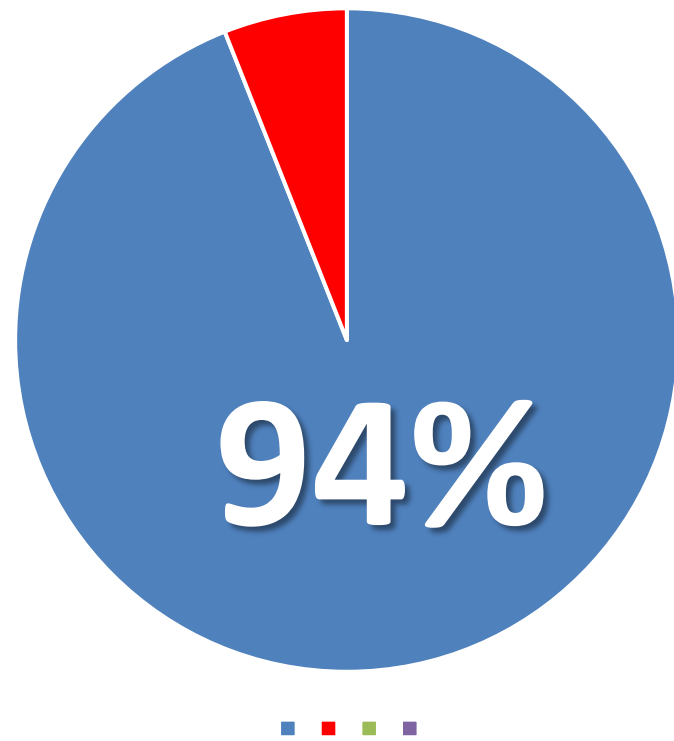
In a matriarchy, **women's authority is recognized by all and is never coercive.** Social management is for the common good. It is a sharing society based on "being" and not on "having". It is structured on the loving values of a "good" mother.

Matriarchy is generally understood as societies in which **a group of women hold political, economic or religious power.**

**Basque** matriarchy: the **woman wears the trousers at home.**



# TEAM





We are  
leading the path  
In Europe



## Since 2018

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**Founded in 2018** and headquartered in Derio (Bizkaia), a bio-pharmaceutical company born to conduct research, develop, and manufacture medicines based on the human microbiome

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## First in class

The company's aim is to **market in 2025** the first biological medicine based on intestinal microbiota in Europe

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## MBK-01

MBK-01 is a **biological medicine** based on intestinal microbiota with FSPIM® technology. Lyophilized **oral capsules** for various indications.

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## Licensing

Production will be carried out by internal sourcing and commercialization will be managed by **license agreements** (currently in ongoing discussions)

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# CLOSTRIDIUM DIFFICILE INFECTION

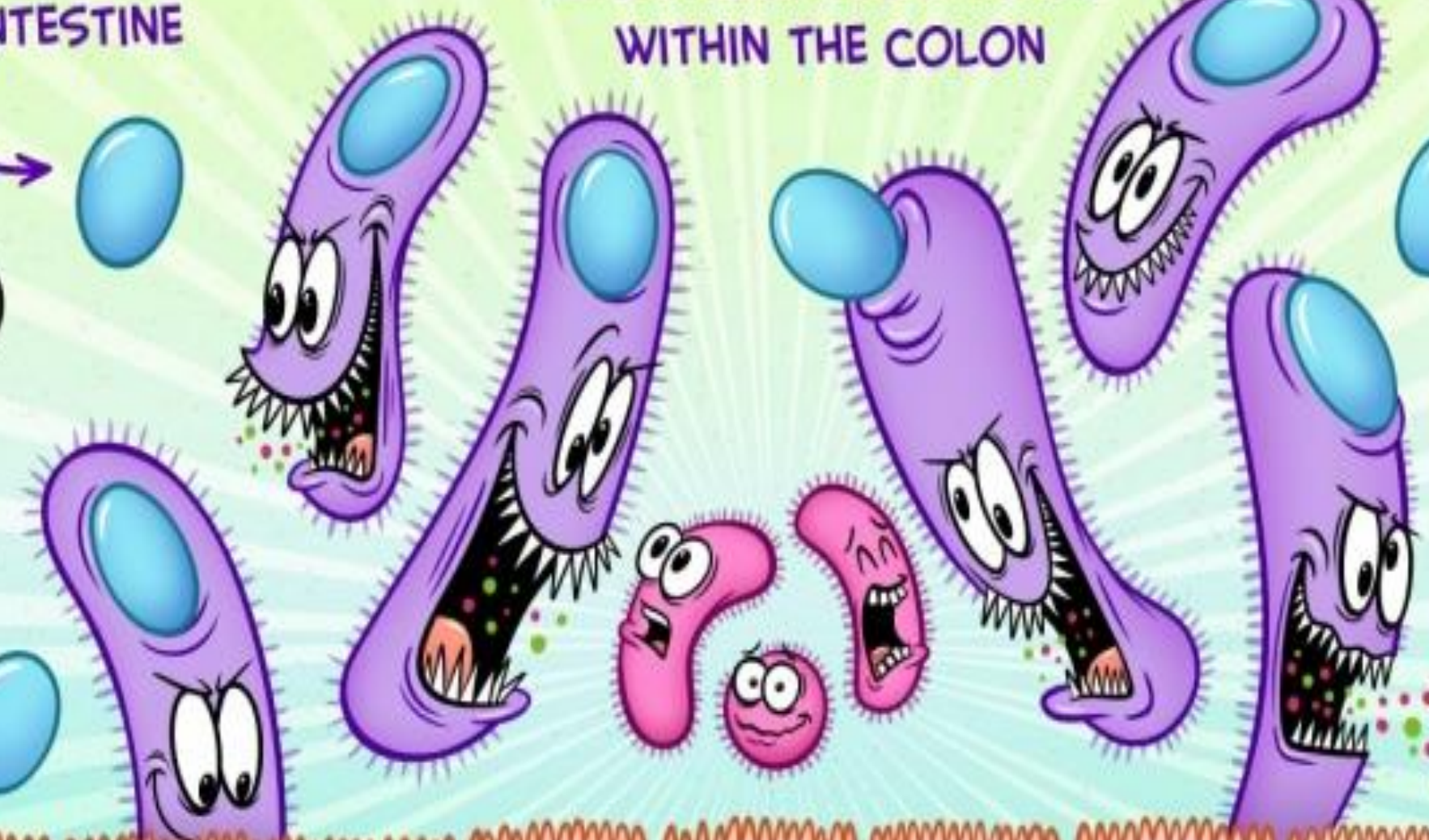
FEVER, CRAMPY ABDOMINAL PAIN, DIARRHEA

MOST COMMON INFECTIOUS CAUSE OF NOSOCOMIAL DIARRHEA

C. DIFFICILE CONTAINS ENDOSPORES THAT CAN SURVIVE THE ACIDITY OF THE STOMACH AND REACH THE LARGE INTESTINE



C. DIFFICILE FLOURISHES WITHIN THE COLON



TOXINS A & B CAUSE MUCOSAL DAMAGE

PSEUDOMEMBRANOUS COLITIS: YELLOWISH PLAQUES FORM OVER DAMAGED EPITHELIUM



THE NORMAL GUT FLORA IS ALTERED BY BROAD-SPECTRUM ANTIBIOTICS, MOST NOTABLY CLINDAMYCIN, CEPHALOSPORINS, AMPICILLIN, AMOXICILLIN, AND FLUOROQUINOLONES







*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

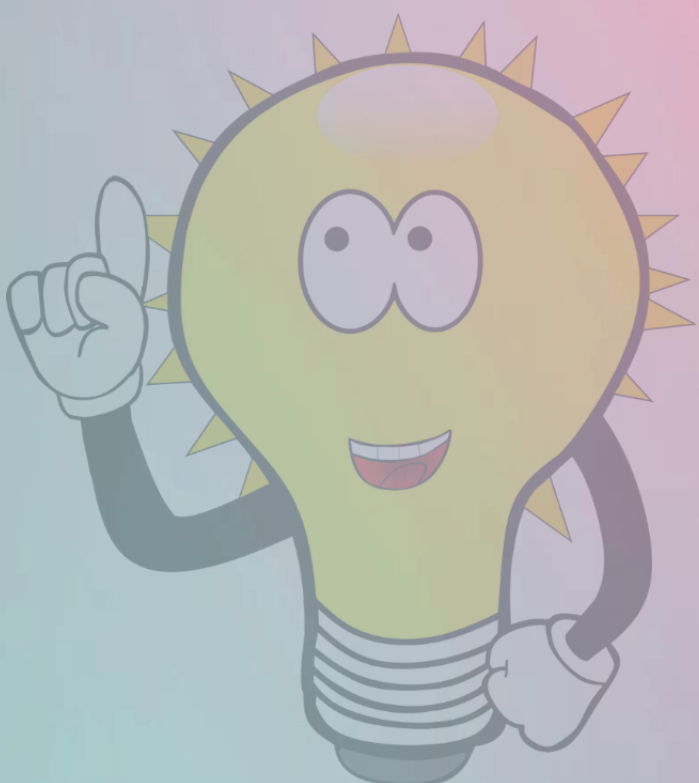
JANUARY 31, 2013

VOL. 368 NO. 5

Duodenal Infusion of Donor Feces for Recurrent  
*Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D.,  
Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D.,  
Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D.,  
Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

The idea







# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JANUARY 31, 2013

VOL. 368 NO. 5

## Duodenal Infusion of Donor *Clostridium di*

Erwin

Vancomicina  
500 mg  
oral/4 veces  
día/ 4 días  
+  
FMT  
nasoduodenal

13/16 (81%)

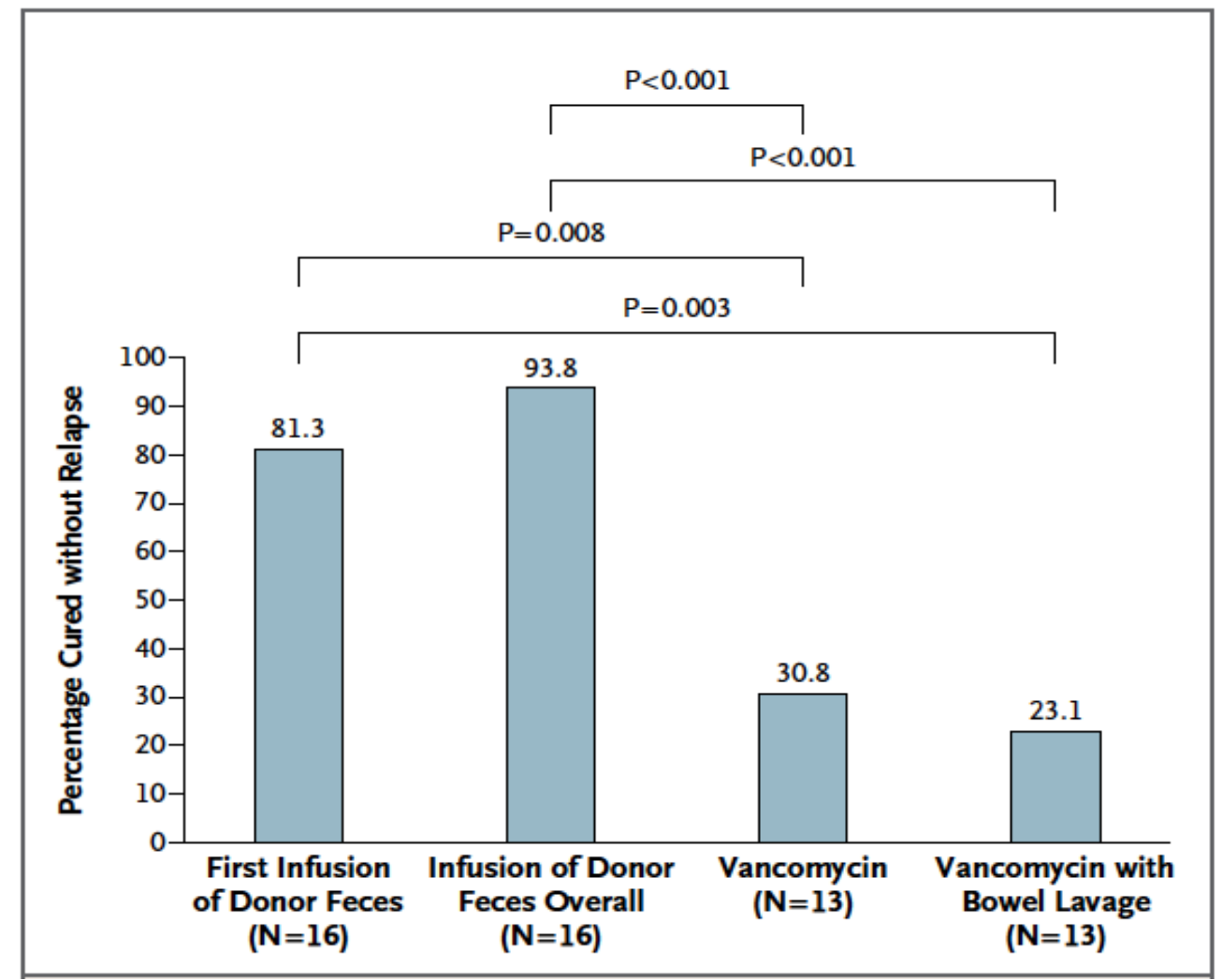
Vancomicina  
500 mg  
oral/4 veces  
día/ 4 días

4/13 (31%)

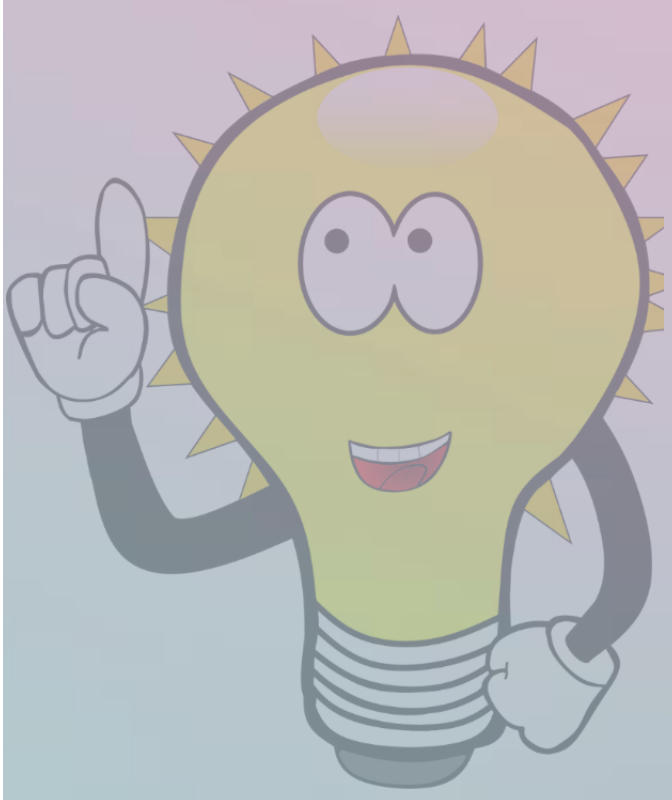
Vancomicina  
500 mg  
oral/4 veces  
día/ 4 días  
+  
Lavado  
intestinal

3/13 (23%)

Nieuwdo  
Caroline E  
Tijssen, P  
, and Josb



# The idea





Mikrobiomik aims with its first investigational medicine, MBK-01, to be the first company to market worldwide the first biological medicine based on intestinal microbiota in the indication of primary & recurrent *Clostridioides difficile*, in an innovative and friendly format of 4 freeze-dried faecal microbiota oral capsules (FSPIM) in a single dose



KEEP IT  
SIMPLE



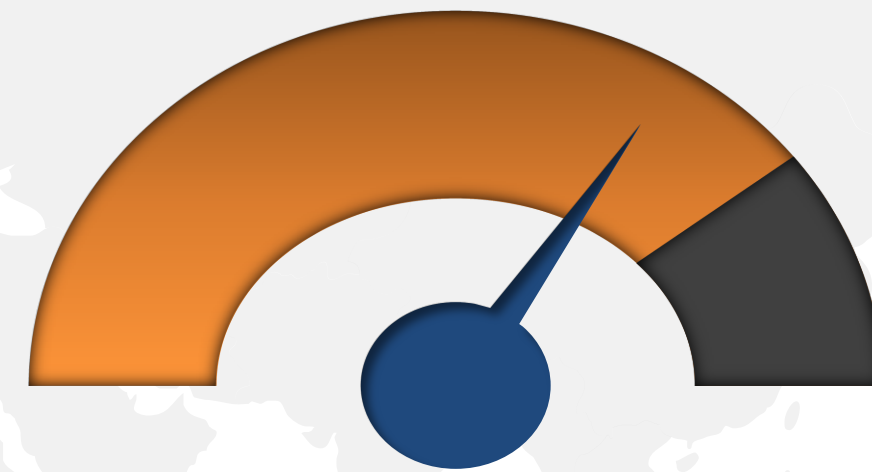
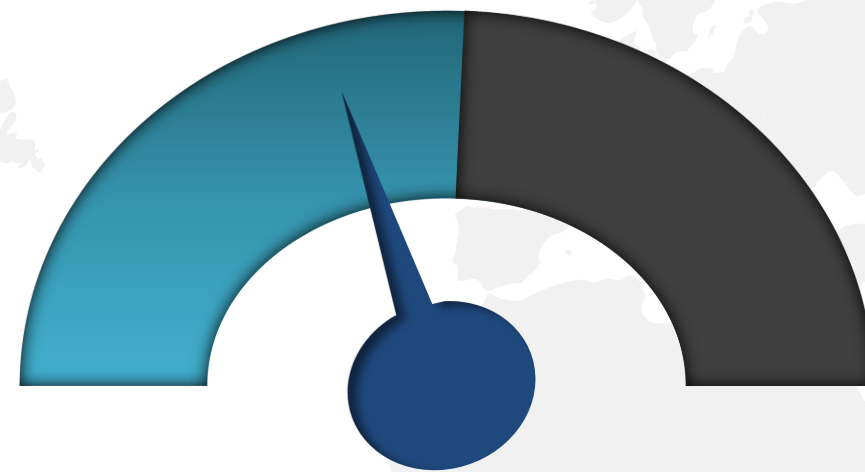
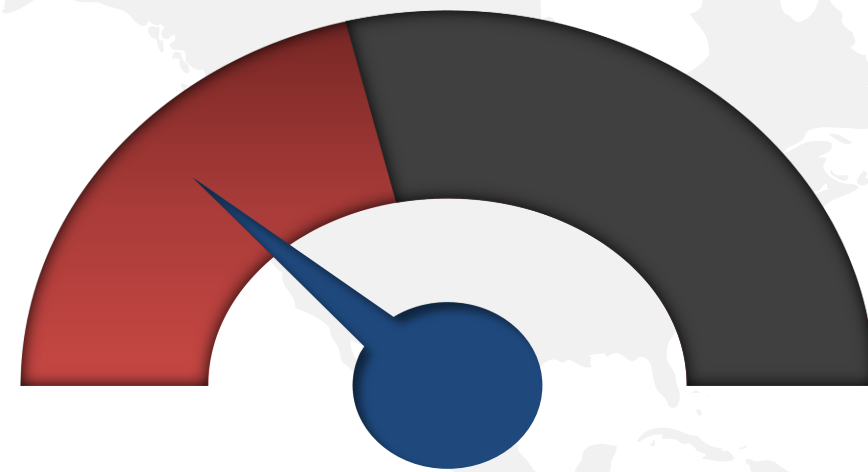


# Keep It Simple

**Product**

**Facility**

**Trial**



**MBK-01**

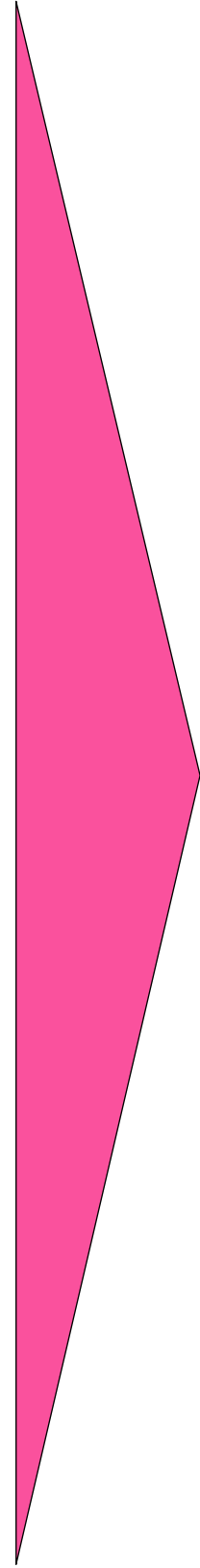
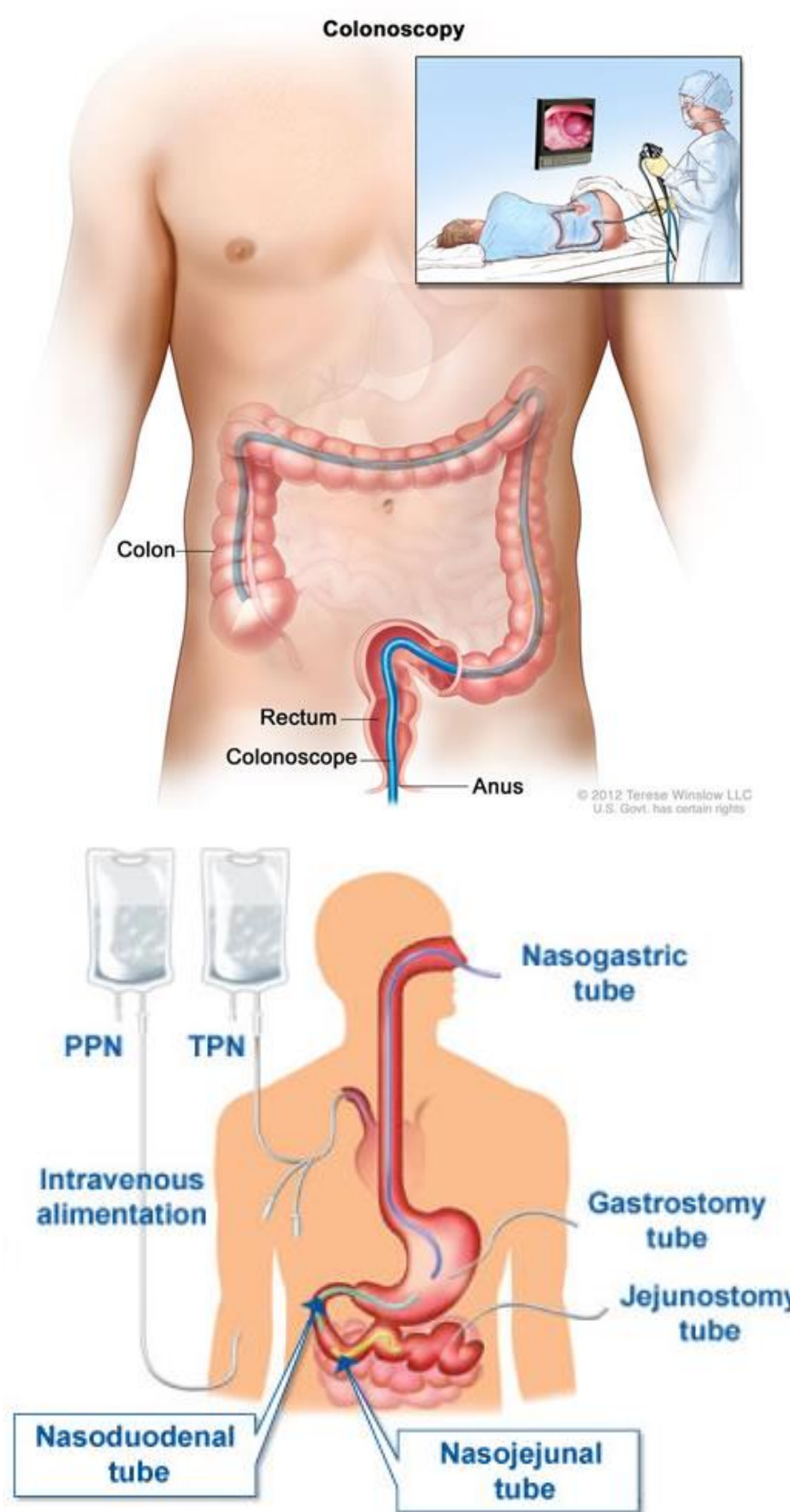
**GMPs**

**PHASE III**





# K I S



**GMP (Good Manufacturing Practices)**





# MY FIRST CONTACT WITH THE MICROBIOME'S SPACE

CUTTING-EDGE TECHNOLOGY

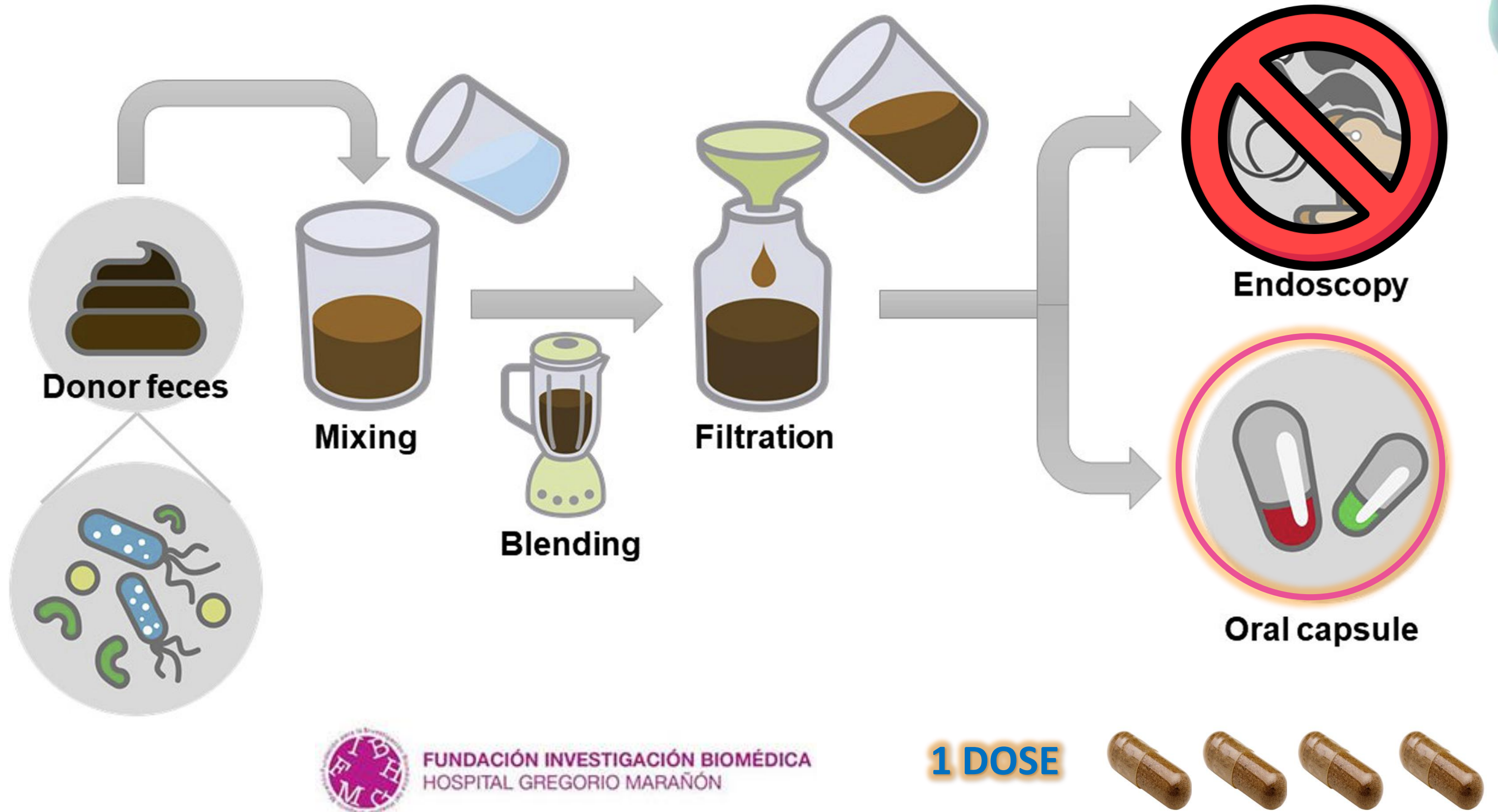




# K

# I

# S



FUNDACIÓN INVESTIGACIÓN BIOMÉDICA  
HOSPITAL GREGORIO MARAÑÓN

**1 DOSE**





**K**

**I**

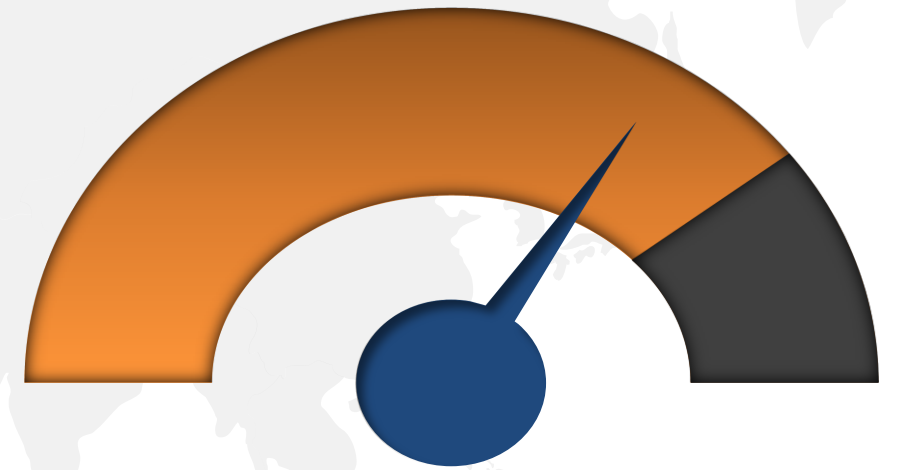
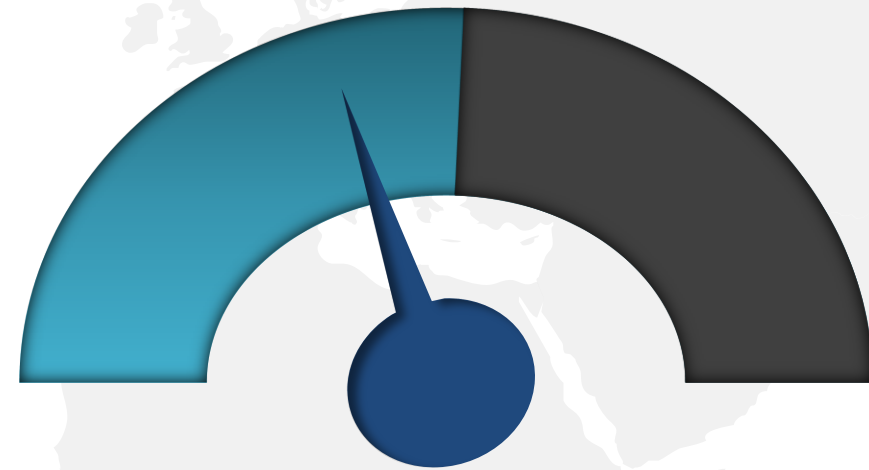
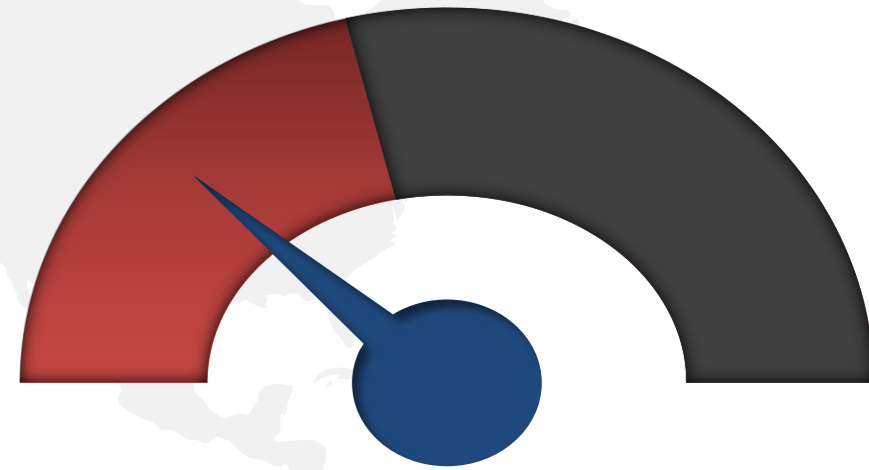
**S**



**Product**

**Facility**

**Trial**



**MBK-01**

**GMPs**

**PHASE III**







**PILOT SCALE GMP  
FACILITY  
(Good Manufacturing  
Practices)**





**K**

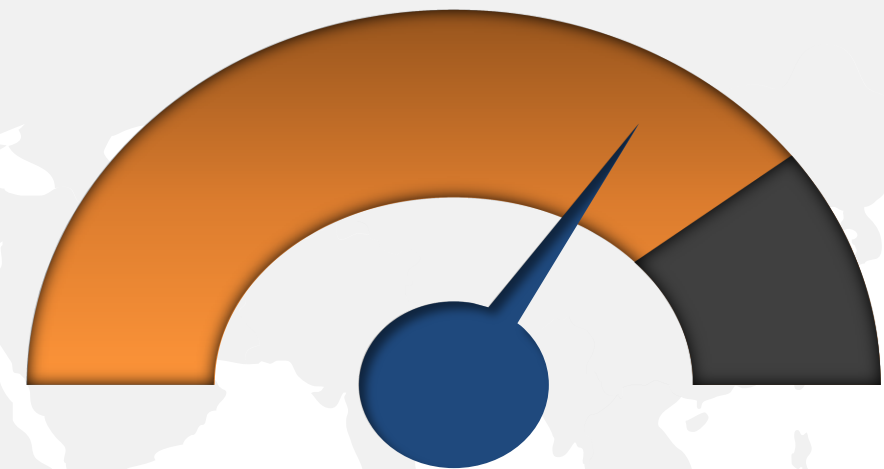
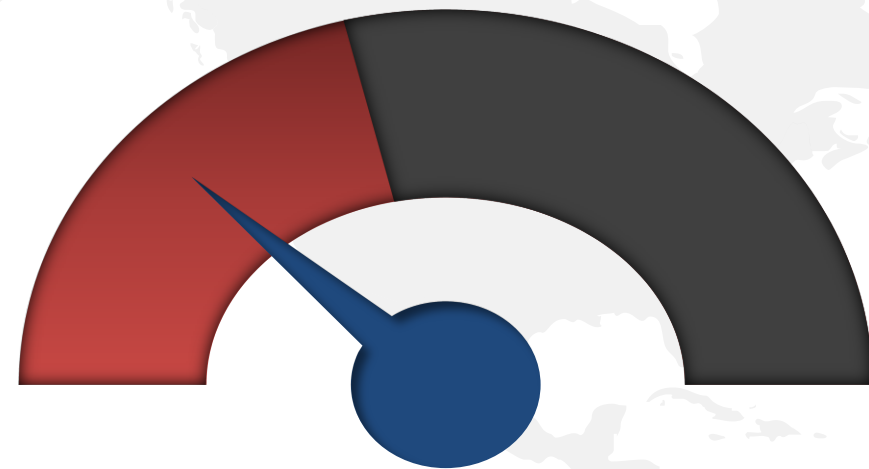
**I**

**S**

**Product**

**Facility**

**Trial**



**MBK-01**

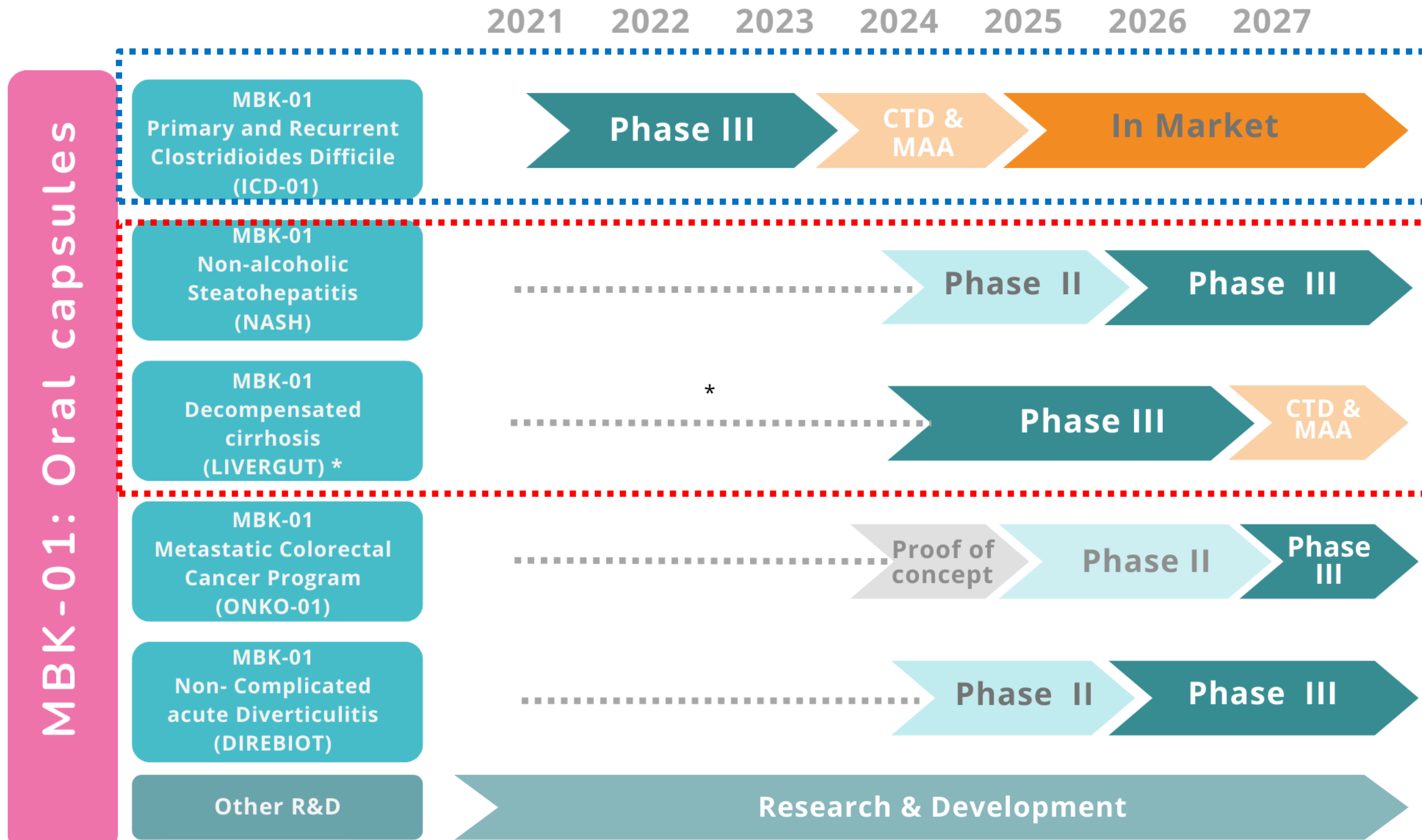
**GMPs**

**PHASE III**





# PIPELINE



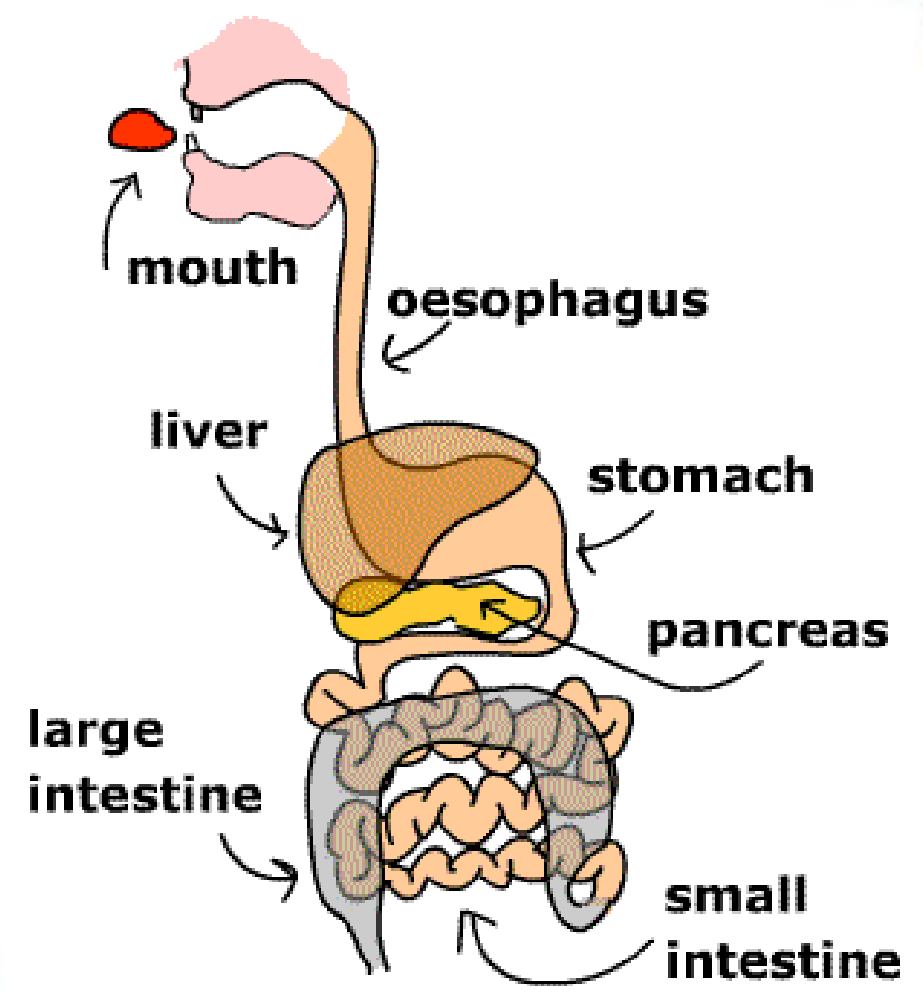
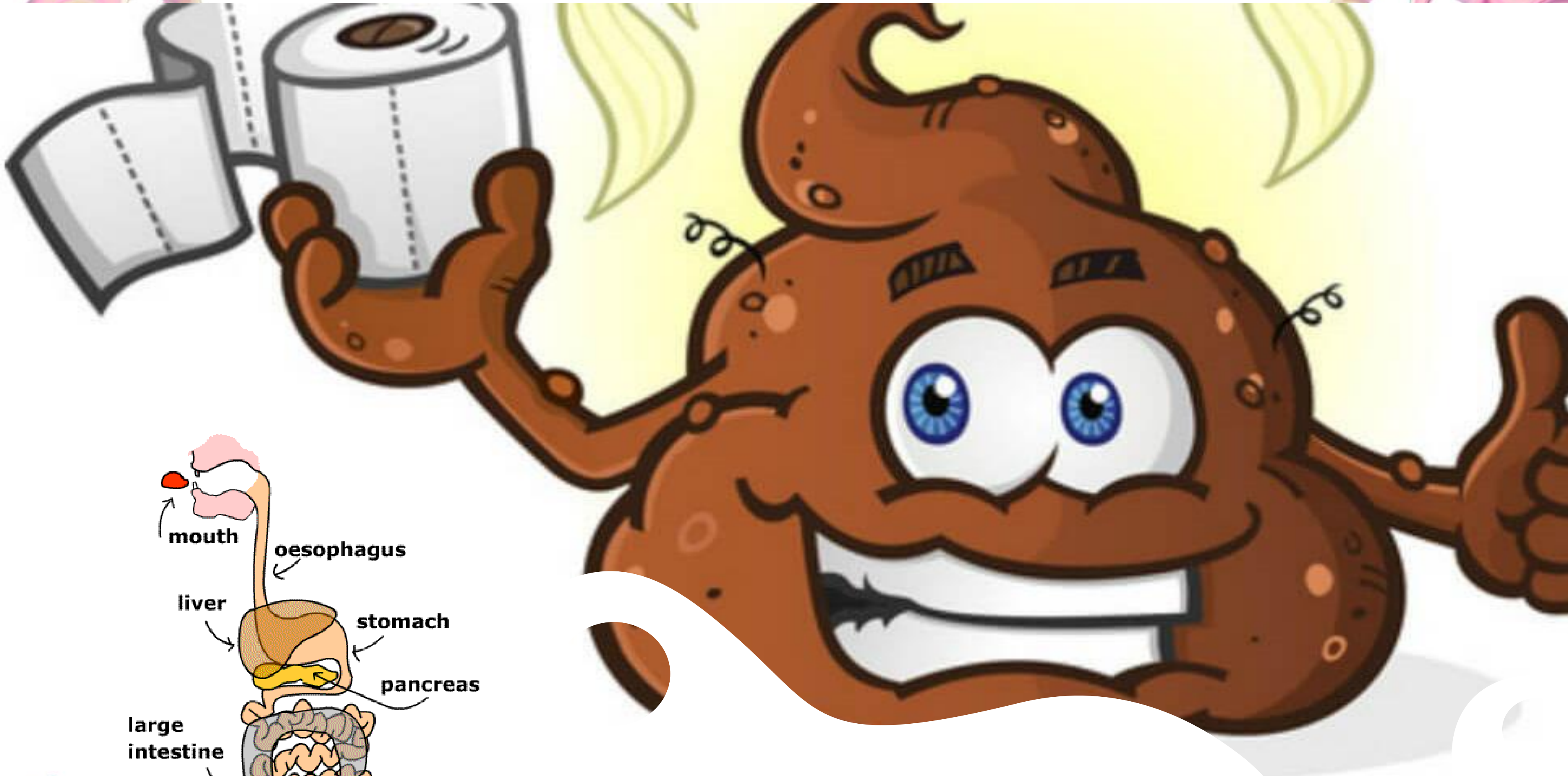
\*Mikrobiomik is not the clinical trial holder.





**We present  
our  
raw material**









**We present  
our  
suppliers**





***STOOL  
DONOR***

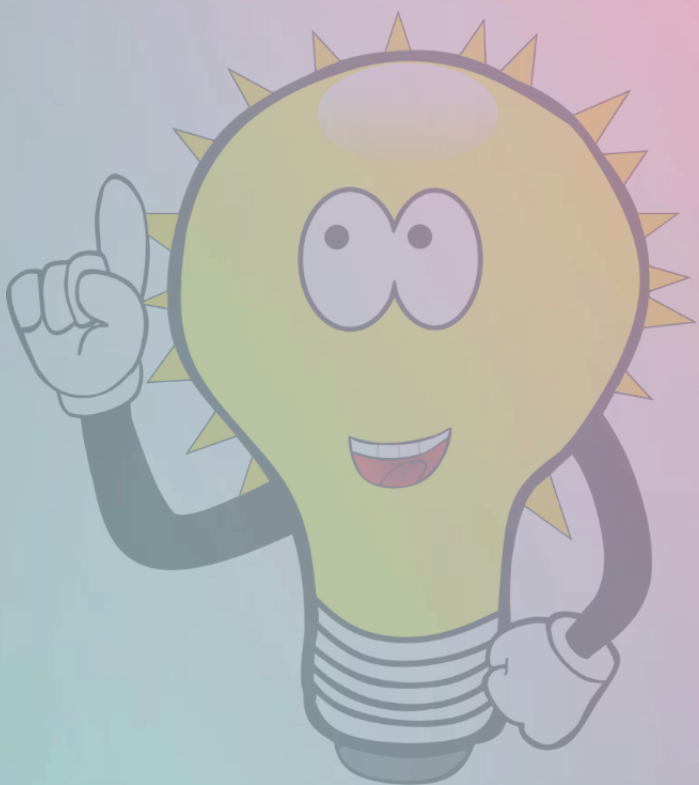


**STOOL  
DONOR**





# The idea



It was hard for doctors to treat patients with the most common hospital-acquired infection, *C. difficile*.

**500,000**

Americans are affected by *C. difficile* each year.

**30**

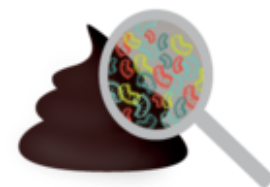
**THOUSAND** patients die from *C. difficile* every year.

**1** in **5** patients with *C. difficile* do not respond to antibiotics



**BUT**

FMT introduces healthy bacteria, curing recurrent *C. difficile* in over **90%** of cases.



so **OPENBIOME** started in 2012 to enable safe access to fecal transplants

since then, we've



Processed over **1300** pounds of stool

passed only

**3%**

of prospective donors through our rigorous screening process

& catalyze research on the microbiome.



Funded **56** pro bono treatments



Supported **3** translational **11** clinical **14** research studies

Covered **96%** of all U.S. residents within 150 miles of an OpenBiome partner



Partnered with **600+** healthcare institutions



across **50** states



Shipped material to **6** countries

Treated over

**13,000**

patients

We aim to turn the tide against *C. difficile*, and help uncover new applications for this exciting treatment.



OPENBIOME

# HOW POOP SAVES LIVES

Fecal transplants step by step

**1**

**Poop Collection**

Feces, also called stool or poop, is collected from a carefully screened, healthy donor.

**2**

**Processing of Donor Poop**

In the lab, the donor poop is mixed with saline solution, then filtered. The finished product contains the good bacteria in a liquid or capsule format.

**3**

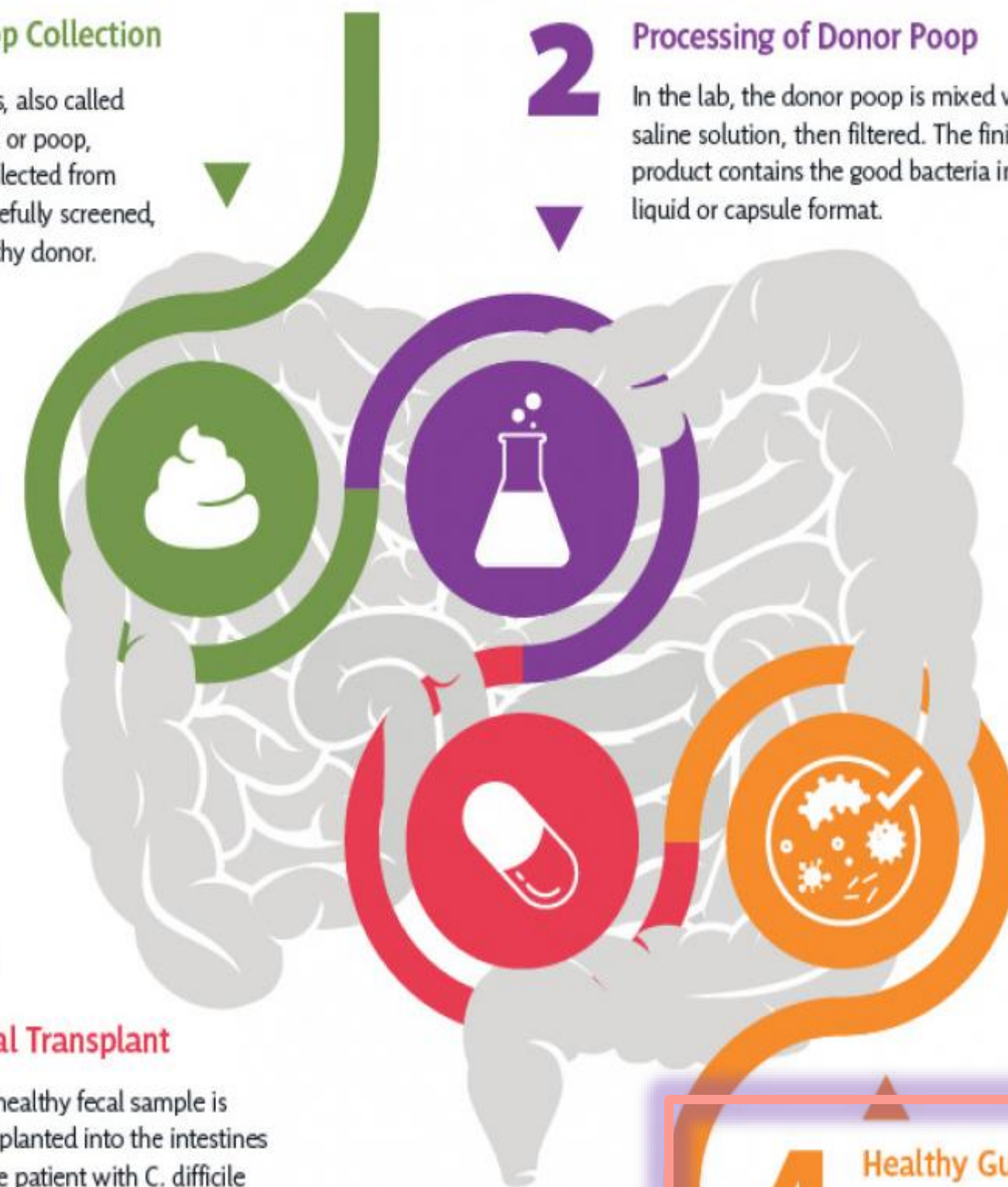
**Fecal Transplant**

The healthy fecal sample is transplanted into the intestines of the patient with *C. difficile* through either an oral route using capsules swallowed by the patient, or the rectal route via enema.

**4**

**Healthy Gut**

The organisms from the donor sample restores the healthy gut bacteria in the patient.







# ICD-01

## Clinical trial

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### A **Randomised, Controlled, Open-label Phase III**

Clinical Trial in Patients With Primary or Recurrent ***Clostridioides Difficile (CD) Infection***, to Evaluate the Efficacy and Safety of MBK-01, Capsules of Lyophilised Faecal Microbiota vs Fidaxomicin

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**21** hospital in Spain

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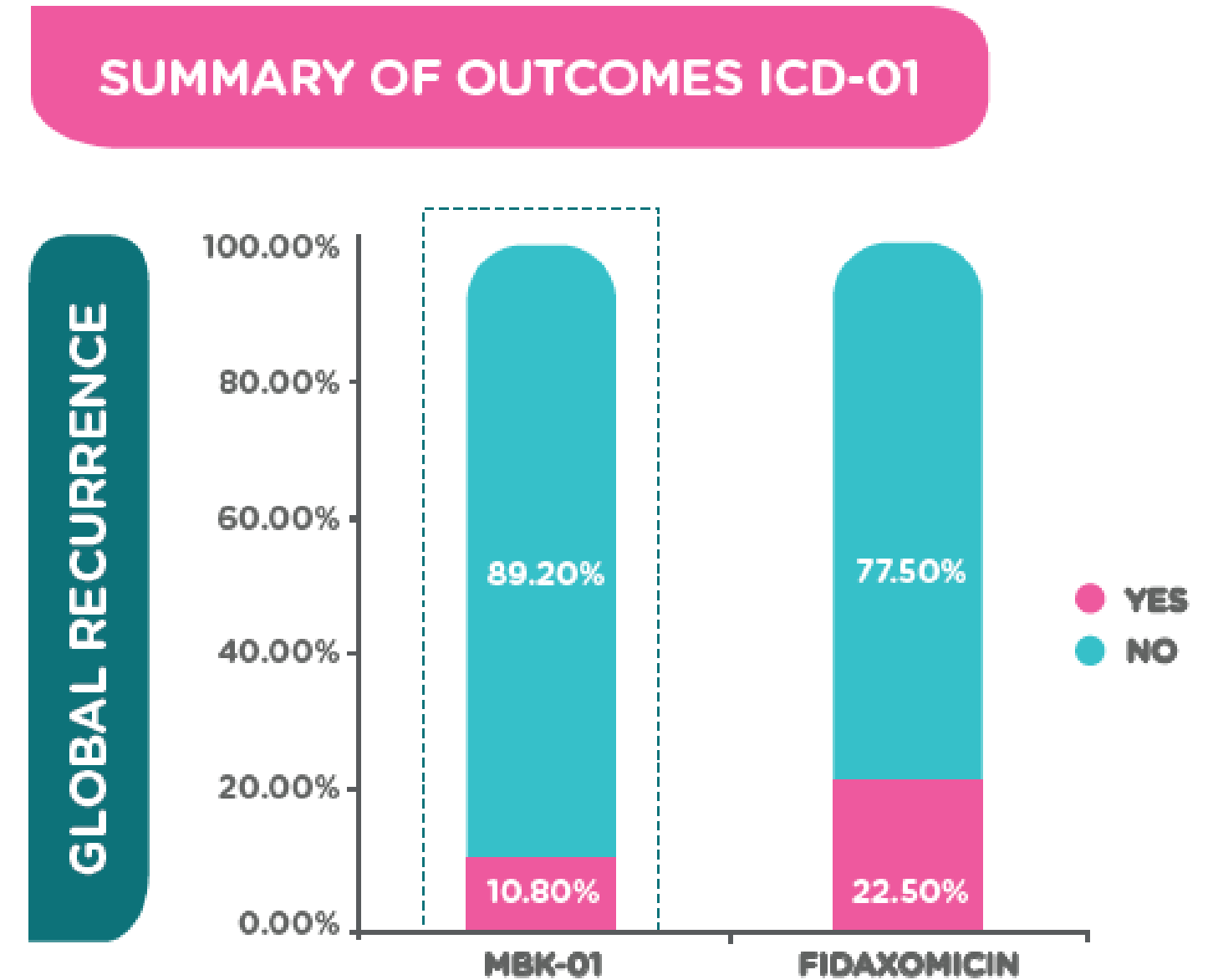
**The aim was to assess the efficacy and safety** of the experimental product MBK-01 compared to fidaxomicin in CDI cases, 8 weeks after the start of the treatment, evaluating the absence of recurrences.



# Outcomes Clinical Trial ICD-01



- ✓ MBK-01 is considered non inferior to Fidaxomicin in efficacy and security in the CDI treatment
- ✓ MBK-01 is considered non inferior to Fidaxomicin for the primary infection in the CDI treatment (1:1)
- ✓ MBK-01 is superior to fidaxomicin for the treatment of recurrent CDI (7:1)
- ✓ The superiority of MBK-01 over fidaxomicin becomes more pronounced as the number of prior recurrences increases
- ✓ MBK-01 is 100% effective in the patients without an antibiotic pre-treatment
- ✓ The treatment with MBK-01 is 100% safe (no SAEs)



PHASE III

# COMPASSIONATE USE

# 53

- EAP (France)
- Compassionate use (Germany)



# COMPETITIVE LANDSCAPE



Product	Composition	Route	Dose	Company	Country	Indication	CT Phase	Comparator	Outcomes	Partners	\$
MBK-01	FSPIM	Oral	4 capsules	Mikrobiomik	Spain	CDI	III Completed	Fidaxomicin	Interim		Last (July 2023) 1.1M€
SER-109 <sup>1</sup>	<i>Firmicutes</i> spores	Oral	4 capsules x 3 days	Seres Therapeutics	USA	rCDI	On market	Placebo	91.3% Clinical response	Nestlé	Upfront \$125M+175M
RBX-2260 <sup>2</sup>	Microbiota suspension	Enema	Enema	Rebiotix	USA	rCDI	On market	Placebo	70.6% Clinical response	-	-
MaaT013	Full spectrum +Butycore	Enema	3 bags	Maat Pharma	France	Gastrointestinal acute Graft-vs-host-Disease	III Ongoing	No (single arm)		-	13M€ (Febrary 2023)
VE-303	8 strains spectrum consortium	Oral	-	Vedanta Biosciences	USA	Severe rCDI	III Completed	Placebo	Meets primary efficacy endpoint Ph II	BMS	Last round \$105M May 2023
EBX-102	Full spectrum	Oral	Capsules	Enterobiotix	UK	Liver cirrhosis and hepatic encephalopathy	II Ongoing	Placebo	-	-	\$21M



### VOWST

4 capsules x 3 days  
rCDI  
Antibiotic pre-treatment

**25%  
of the  
market**



### MBK-01

4 capsules x 1 day  
Primary & rCDI  
**No antibiotic pre-treatment**

**100%  
of the market**



### REBYOTA

Enema  
rCDI  
Antibiotic pre-treatment

**25%  
of the  
market**

# COMPETITIVE LANDSCAPE





**1. Mikrobiomik in a nutshell**

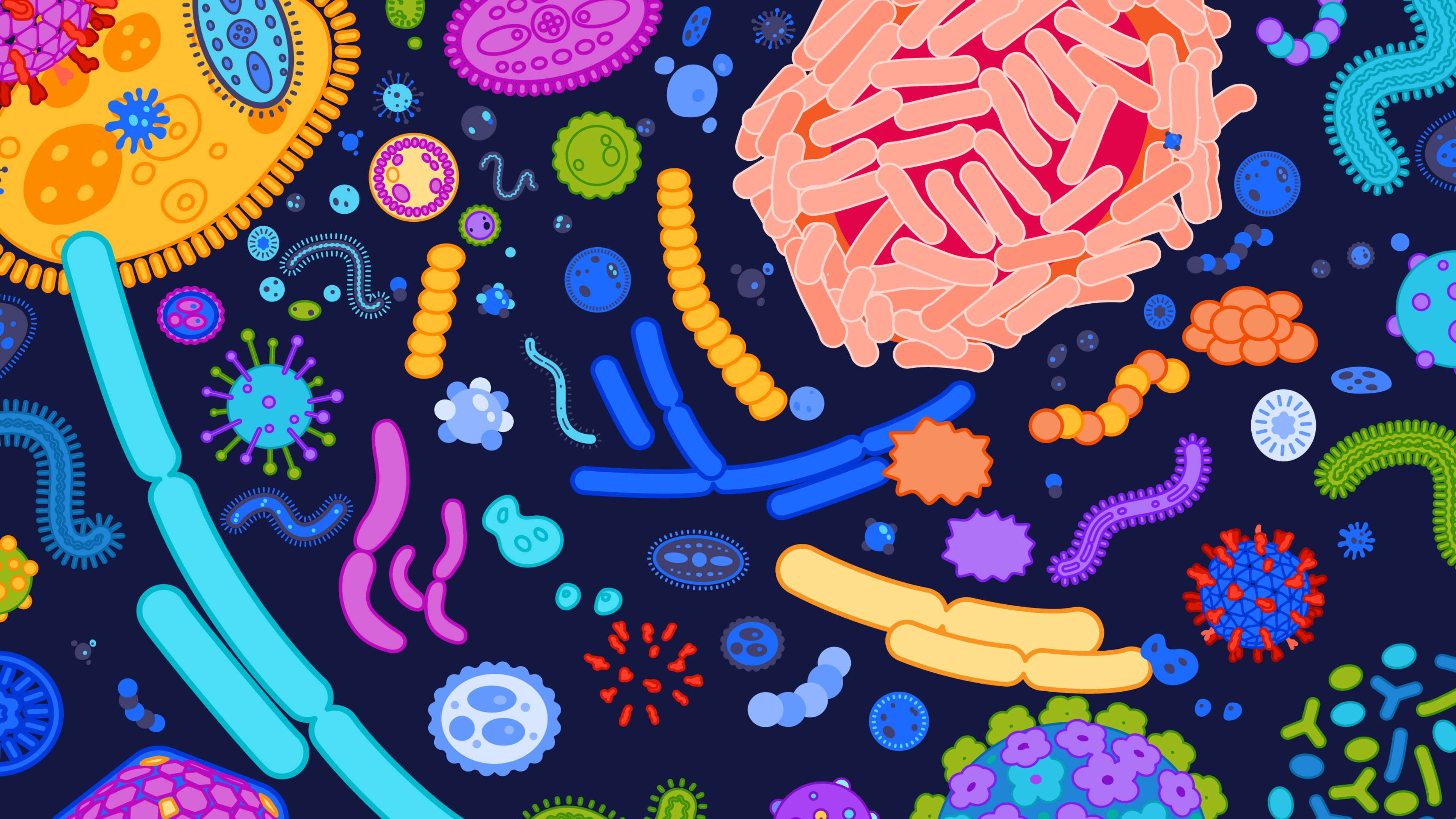
**2. MASH & FSPIM**

**3. EMOTION phase II clinical trial**

**4. LIVERGUT phase III clinical trial**

**5. Take a home message**







The background of the slide features a dense field of teal-colored, rod-shaped bacteria, likely representing the microbiome. The bacteria are rendered with a slight 3D effect and are scattered across the entire frame, creating a textured, scientific backdrop.

**1. Mikrobiomik in a nutshell**

**2. MASH & FSPIM**

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# EMOTION

## Phase II Clinical trial

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**Randomized, double-blind,  
multicenter** study (4 sites)

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Evaluate the **efficacy, safety,**  
and **tolerability** of fecal  
microbiota transplantation via  
oral capsules (MBK-01) vs  
placebo

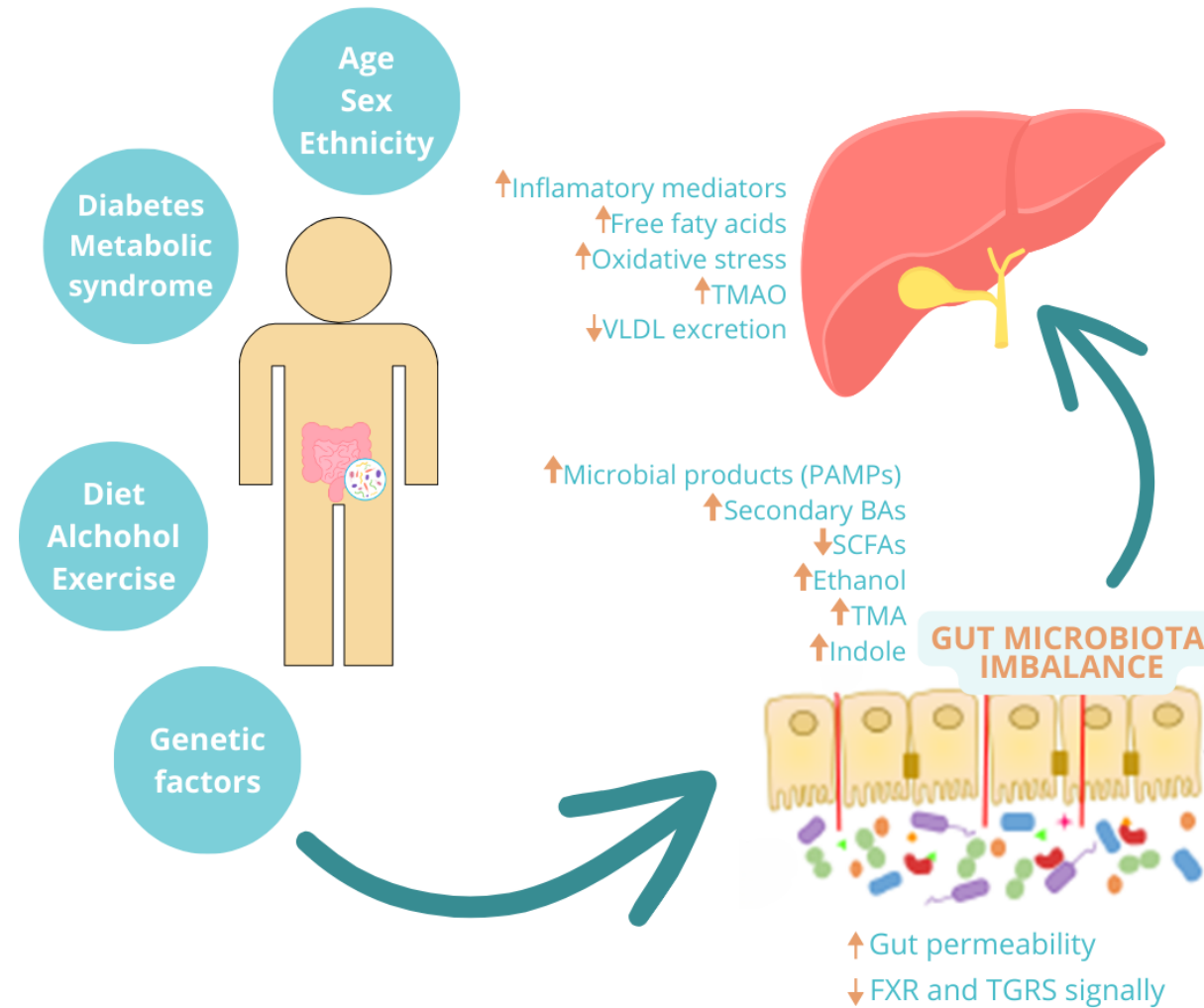
---

For the treatment of **patients**  
with **non-alcoholic  
steatohepatitis**, now MASH





## Different factors affect the gut microbiome



- **Gut microbial imbalance** causes an increase in secondary bile acids, which modulates **FXR and FGR5 signaling**, affecting the **glucose and lipid metabolism** and **anti-inflammatory immune response**
- The **increase in certain microbial metabolites** mediates weakening of **intestinal tight junction**, enabling passage to the systemic circulation of PAMPs and microbial metabolites (such as **ethanol**) that reach the liver inducing inflammatory responses, liver injury and fibrosis.

EMOTION

Phase II  
Clinical trial



# PRIMARY OBJECTIVE

Test the **efficacy** of the **faecal microbiota transference** compared to control treatment (placebo) after 72 weeks of treatment initiation. Together with these objectives we test the **security** and **tolerability** of MBK-01 during 72 weeks of treatment.

## EMOTION

Clinical trial

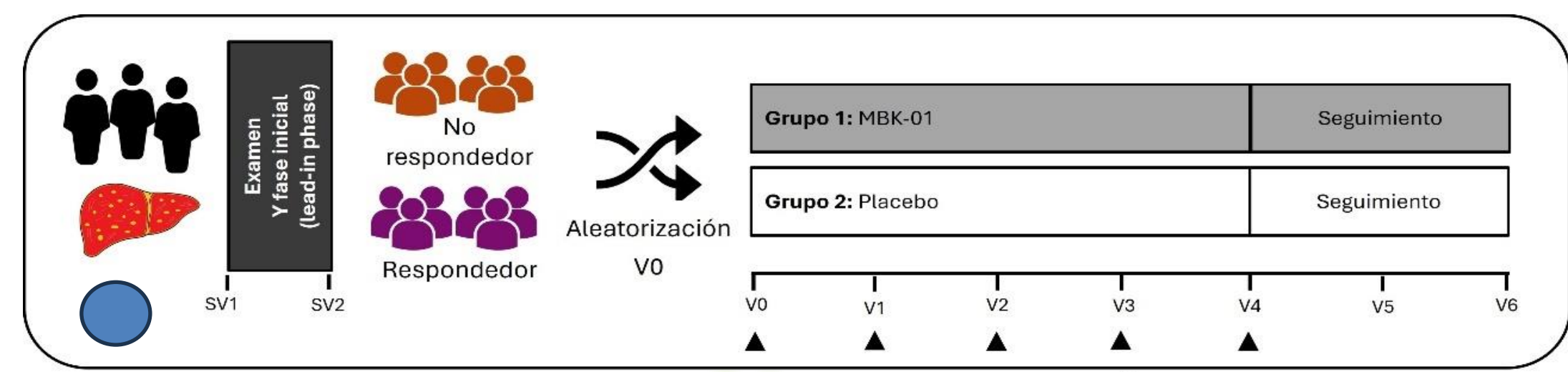
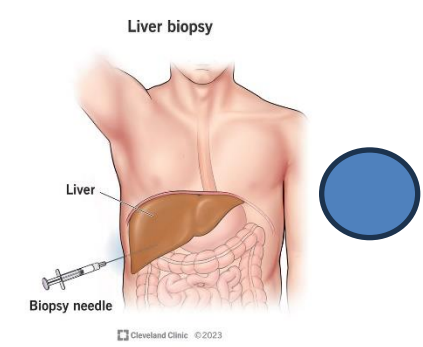
# STUDY POPULATION

**96 patients (2:1)**

### Criteria

- ✓ Male and female patients aged between 18-75 years.
- ✓ Body mass index (BMI) <40 kg/m<sup>2</sup>.
- ✓ Histological diagnosis of MASH from **liver biopsy**.
- ✓ **MASH histological activity score (MAS) ≥ 4**, with a score of **1 or more in each subcomponent** (steatosis, lobular inflammation, and hepatocyte ballooning).
- ✓ **Histological evidence of fibrosis at stage 1, 2 or 3** (MASH CRN fibrosis score).
- ✓ Fertile men and women must use contraceptive measures.

# STUDY DESIGN



**24**  
**12**

Efecto terapéutico, seguridad y tolerabilidad

w85

\*Aleatorización estratificada por presencia de DM2 y fibrosis

▲ Tratamiento / Placebo



The background of the slide is a teal color with a pattern of various rod-shaped bacteria, some appearing to be in motion or interacting. The bacteria are rendered in a semi-transparent, 3D style, giving them a realistic appearance.

**1. Mikrobiomik in a nutshell**

**2. MASLD & FSPIM**

**3. EMOTION phase II clinical trial**

**4. LIVERGUT phase III clinical trial**

**5. Take a home message**



# LiverGut

Phase III  
Clinical trial

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**Randomized  
Double-blinded  
Placebo-Controlled** study (8 sites)

---

For the treatment of **patients** with  
**decompensated cirrhosis**

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**Liver cirrhosis** is the end-stage of  
chronic liver diseases

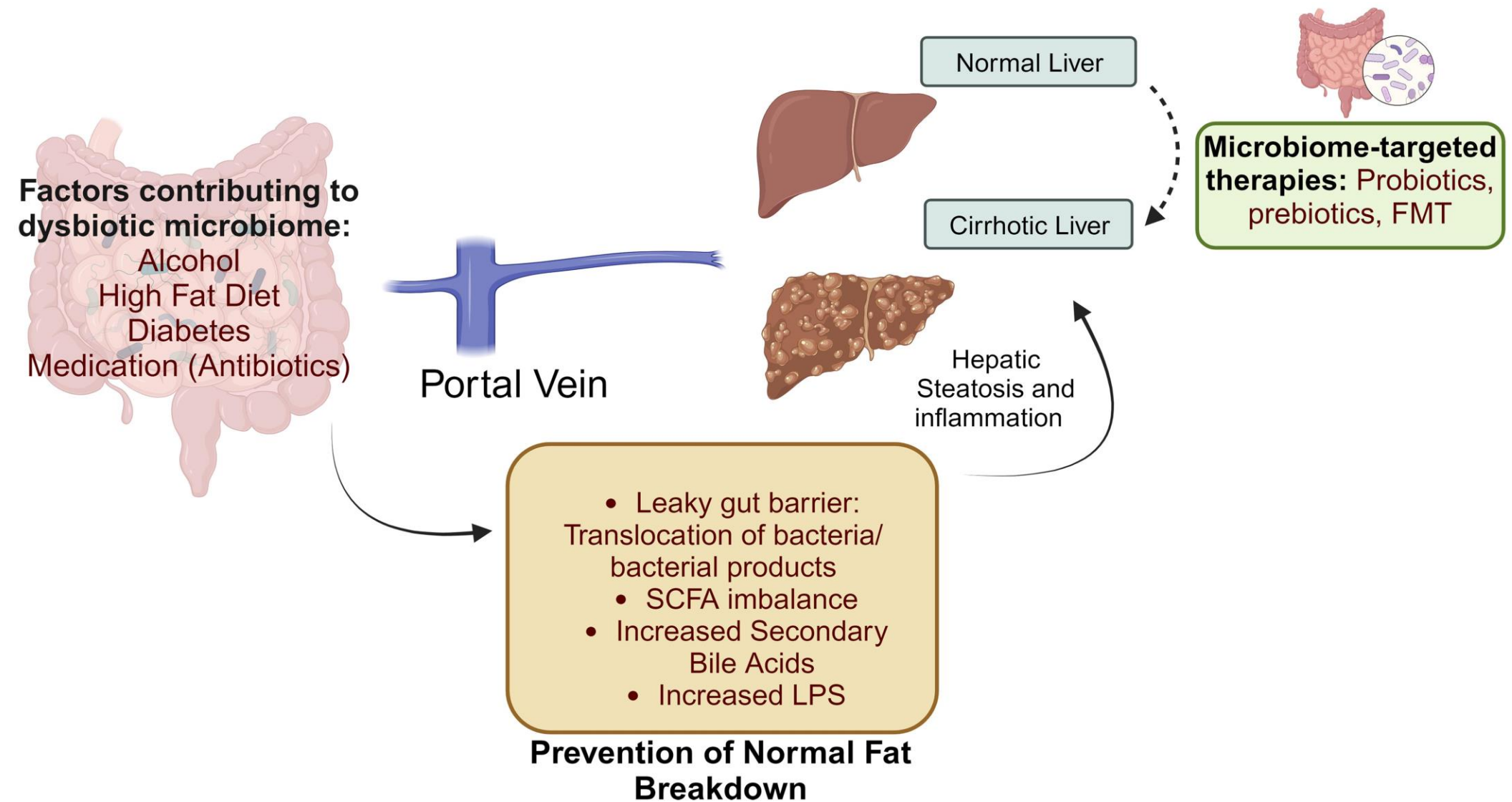
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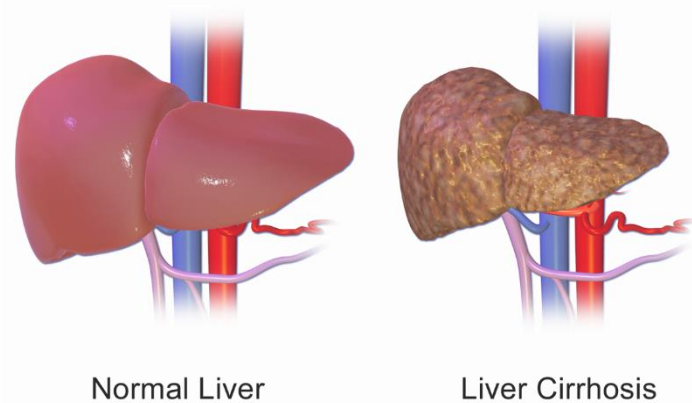
The **gut-liver axis** has a critical role  
in the pathogenesis of cirrhosis  
progression and its complications,  
because liver cirrhosis is associated  
with profound **alterations in gut  
microbiota**



# Fecal Microbiome Transplantation (MBK-01) in Cirrhosis. Randomize Double-blinded, Placebo-Controlled trial in patients with decompensated cirrhosis (LiverGut)

- Liver cirrhosis is the **end-stage** of chronic liver diseases
- The natural course of cirrhosis is characterized by an asymptomatic phase, followed by a **decompensated phase**, characterized by occurrence of **complications**, typically ascites, gastrointestinal bleeding, hepatic encephalopathy (HE), and/or jaundice
- **Portal hypertension** (PH) has been classically considered as the main pathogenic mechanism of complications of cirrhosis
- The **gut-liver axis** has a critical role in the pathogenesis of cirrhosis progression and its complications, because liver cirrhosis is associated with **profound alterations in gut microbiota**
- Currently, there is no specific and effective treatment able to cure or to slow down the progression of the disease. **FMT would restore the microbial community** in patients with compensated and decompensated cirrhosis that would halt the progression of the disease, complications, and mortality





# LiverGut

Phase III  
Clinical trial

## PRIMARY OBJECTIVE

Assess the **safety and efficacy** of fecal microbiota transplantation (MBK-01) from healthy subjects to patients with decompensated cirrhosis as assessed by **preventing new decompensated events**

## STUDY POPULATION

**196 patients (1:1)**

### Criteria

- ✓ Male and female patients  $\geq 18$  years.
- ✓ **Cirrhosis defined by standard clinical criteria, ultrasonographic findings and/or histology.**
- ✓ **Child-Pugh B or C patients (7- up to 12 points).**
- ✓ Women of child-bearing potential must have a negative pregnancy test in serum.
- ✓ Fertile men and women must use contraceptive measures.

- ✓ Currently, **there is no specific and effective treatment** able to cure or to slow down the progression of the disease

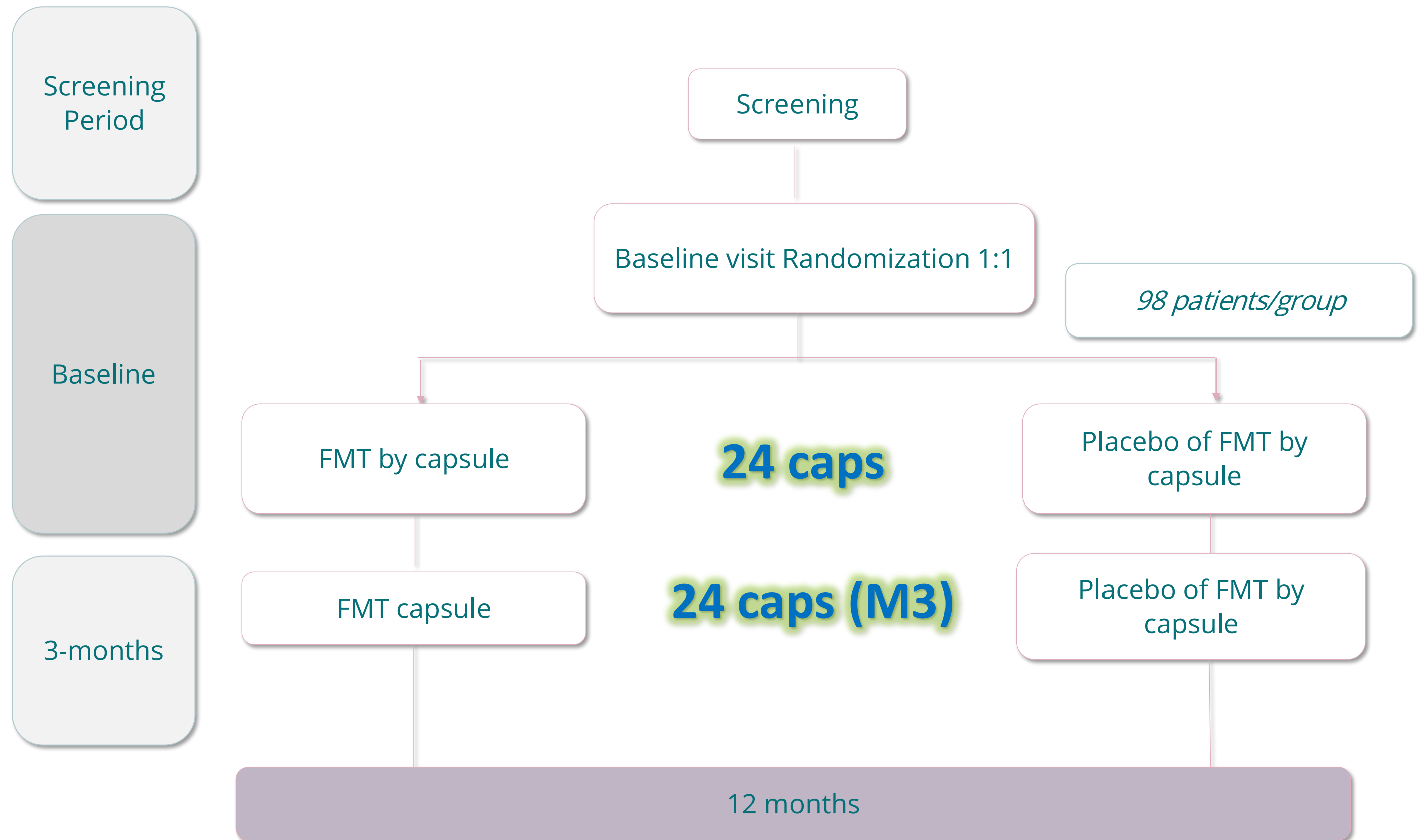




# STUDY DESIGN

## LiverGut

### Phase III Clinical trial



The background of the slide is a teal color with a pattern of various rod-shaped bacteria, likely representing the gut microbiome. The bacteria are rendered in a semi-transparent, 3D style, scattered across the frame.

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**2. MASLD & FSPIM**

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**5. Take a home message**





**REGULATORY AGENCIES**

The background of the image is a teal color with a pattern of various rod-shaped bacteria, some appearing as chains and others as individual cells, rendered in a semi-transparent, light teal color. The main text is centered and reads: 

# Let's keep saving lives through the microbiota!

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[jbasterra@mikrobiomik.net](mailto:jbasterra@mikrobiomik.net)

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[www.mikrobiomik.net](http://www.mikrobiomik.net)



**WHAT IS THIS?**  
**2018**



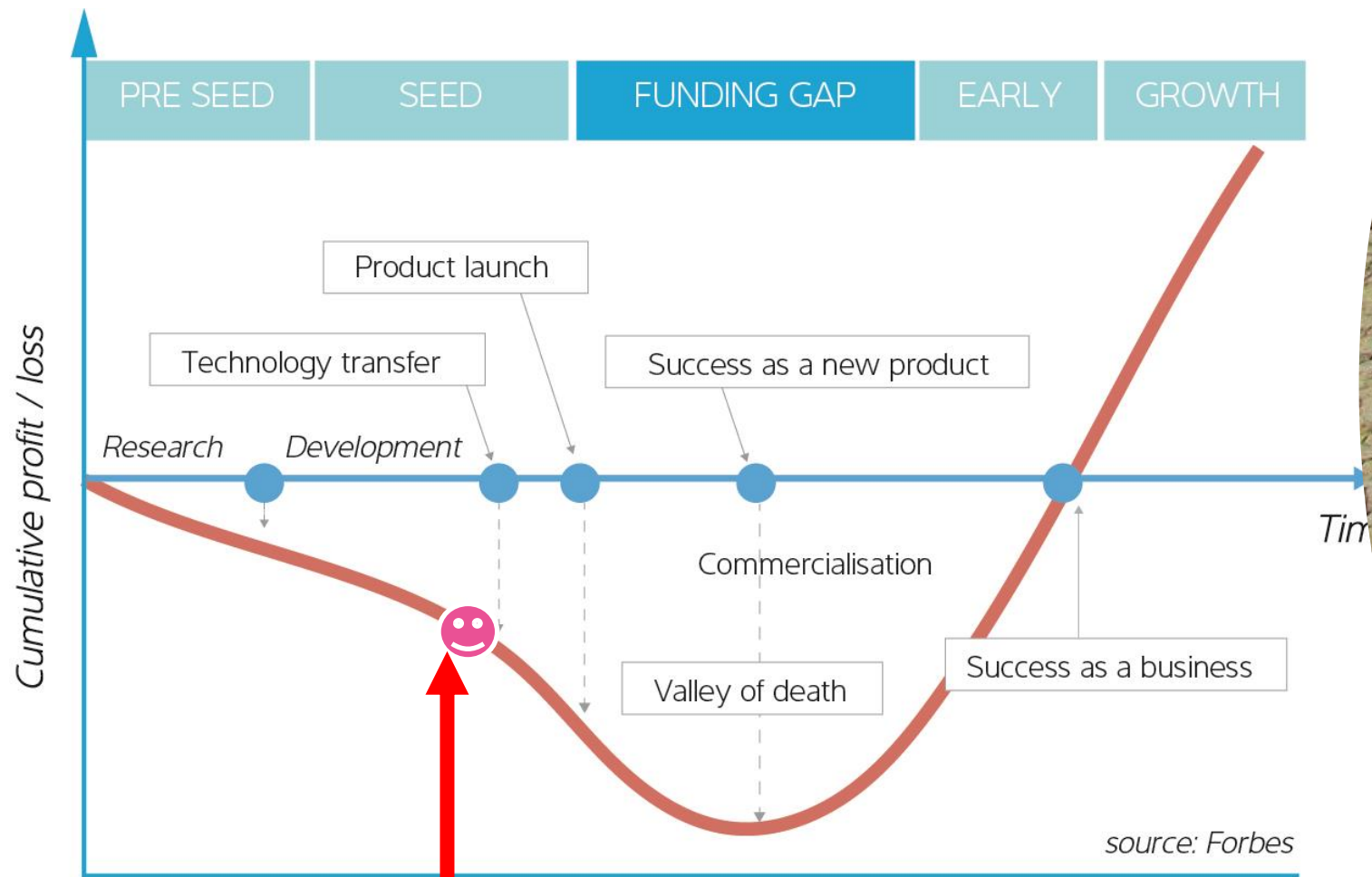
**SUBMISSION CTD**  
**2024**



**REGULATORY AGENCIES**

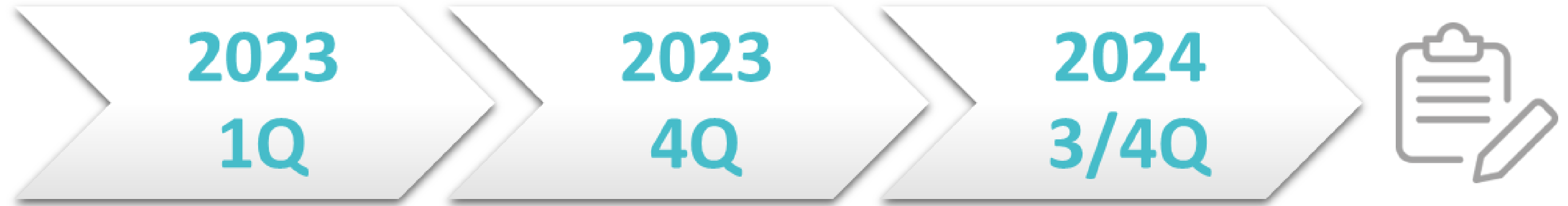


# REGULATORY AGENCIES





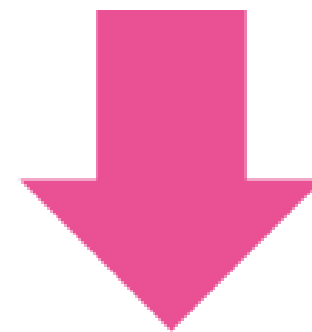
# REGULATORY AGENCIES



Presentation  
of ICD-01  
clinical trial  
interim results

Final results of the  
ICD-01 clinical trial

Finalization of the  
regulatory dossier  
and MA (Marketing  
Authorization).



**3Q 2023**  
**MBK-01: granted as new active  
sustance through centralized  
prodecure by the EMA**



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Inicio redacción del IMPD y protocolo del ensayo clínico		Enero 2021
Presentado el estudio EMOTION (NASH-001) por vía CTIS, el nuevo portal europeo de ensayos clínicos		24/03/2022
Respuesta de la AEMPS: <b>40 consideraciones</b>		04/05/2022
Respuesta a las aclaraciones en el plazo obligatorio e inclusión de nuevos documentos complementarios		13/05/2022
<b>ACEPTADO CON CONDICIONES:</b> (SUPONEN UNA MODIFICACIÓN SUSTANCIAL) <ol style="list-style-type: none"> <li>1. Metagenómica</li> <li>2. Determinación de proteobacterias</li> <li>3. Determinación de impurezas de DNA humano y bacteriófagos</li> <li>4. Variabilidad entre lotes</li> </ol>		10/06/2022
<b>Condición 1 y 2</b>		<b>Condición 3 y 4</b>
<b>Aceptada por Mikrobiomik.</b> Nos ponemos en marcha para realizar los análisis de metagenómica y determinación del % de las distintas poblaciones	Junio 2022	Se prepara y envía a la AEMPS un documento <b>rebatiendo</b> estas 2 cuestiones Responde la AEMPS reiterando su resolución
Búsqueda y homologación de <b>nuevo proveedor</b> con criterios de calidad para realizar con el mismo 3 tipos de análisis: <ul style="list-style-type: none"> <li>– Metagenómica</li> <li>– % de distintas poblaciones (proteobacterias)</li> <li>– Determinación de impurezas de DNA</li> </ul>	Septiembre - Octubre 2022	<b>Reunión con la AEMPS</b> Les convencemos sobre la no necesidad de determinar bacteriófagos y sobre de administrar distintos lotes a un mismo paciente
		29/07/2022 30/08/2022
		21/09/2022



Cambios en el sistema de calidad, IMPD y IB para solventar las consideraciones. <b>Presentación nuevo IMPD</b>	Diciembre 2022
<b>Nuevas aclaraciones</b> y respuesta a las mismas	Marzo 2023
Dictamen tácito de la modificación sustancial AEMPS confirma que tenemos que presentar otra modificación sustancial para responder a las últimas condiciones	Mayo 2023
Se vuelve a enviar los cambios requeridos por la modificación sustancial	Noviembre 2023
Modificación No-sustancial, compromiso adquirido por Mikrobiomik	Marzo 2024
Mikrobiomik <b>modifica</b> el acondicionamiento, y por tanto la <b>caducidad</b> del producto, y debe actualizar el IMPD a través de una modificación sustancial	Mayo 2024

1. Metagenomics
2. Determination of proteobacteria
3. Determination of human DNA impurities and bacteriophages
4. Batch-to-batch variability

We convince them that there is no need to determine bacteriophages and to administer different batches to the same patient.

Changes to the quality system, IMPD and IB to address the considerations.

**Presentation of new IMPD**

December 2022

**Further clarifications** and response to clarifications

March 2023

Tacit opinion of the substantial modification.

AEMPS confirms that we have to submit another substantial modification to meet the latest conditions.

May 2023

Resubmission of changes required by the substantial modification

November 2023

Non-substantial modification, commitment made by Mikrobiomik

March 2024

**Mikrobiomik modifies the packaging, and therefore the shelf life of the product,** and must update the IMPD through a substantial modification.

May 2024