

MaaT  
Pharma

# MaaT Pharma Microbiota as a Therapy

September 2023

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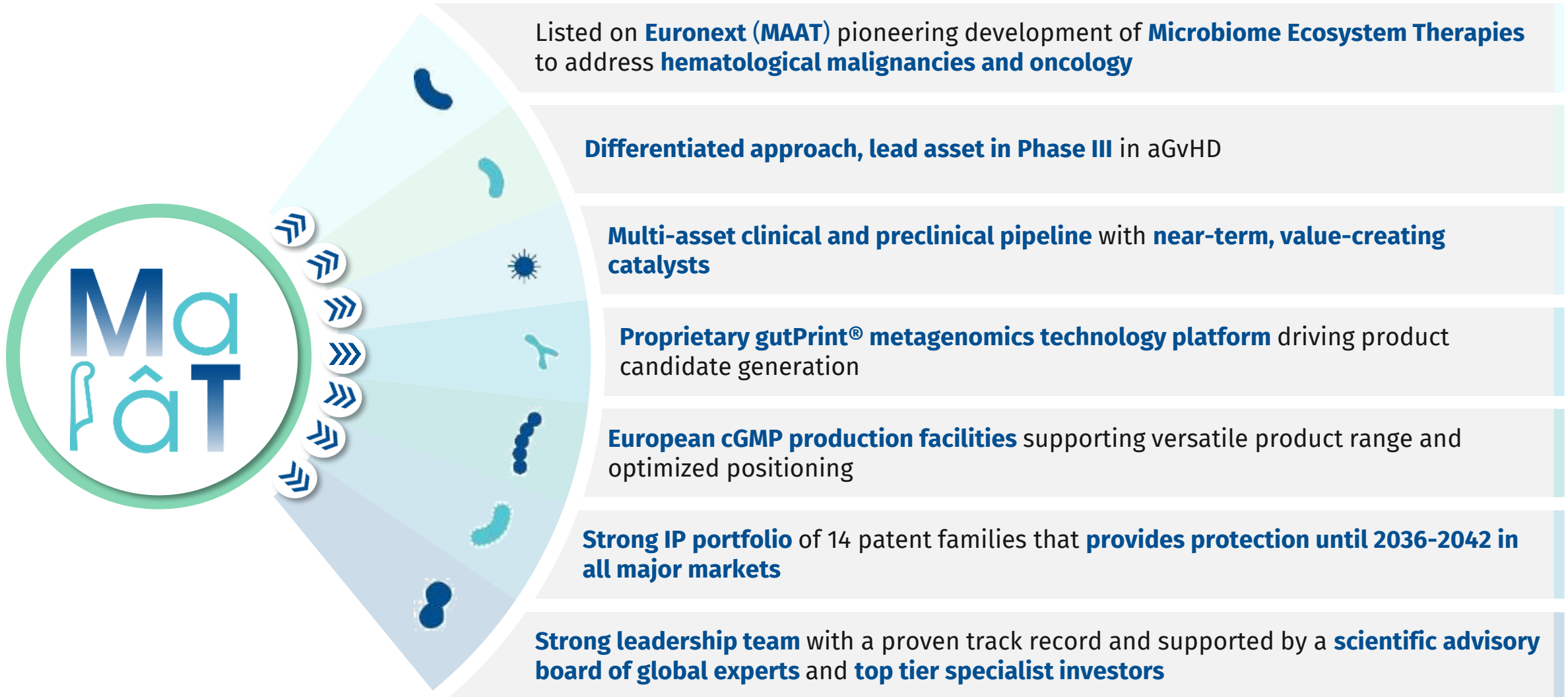
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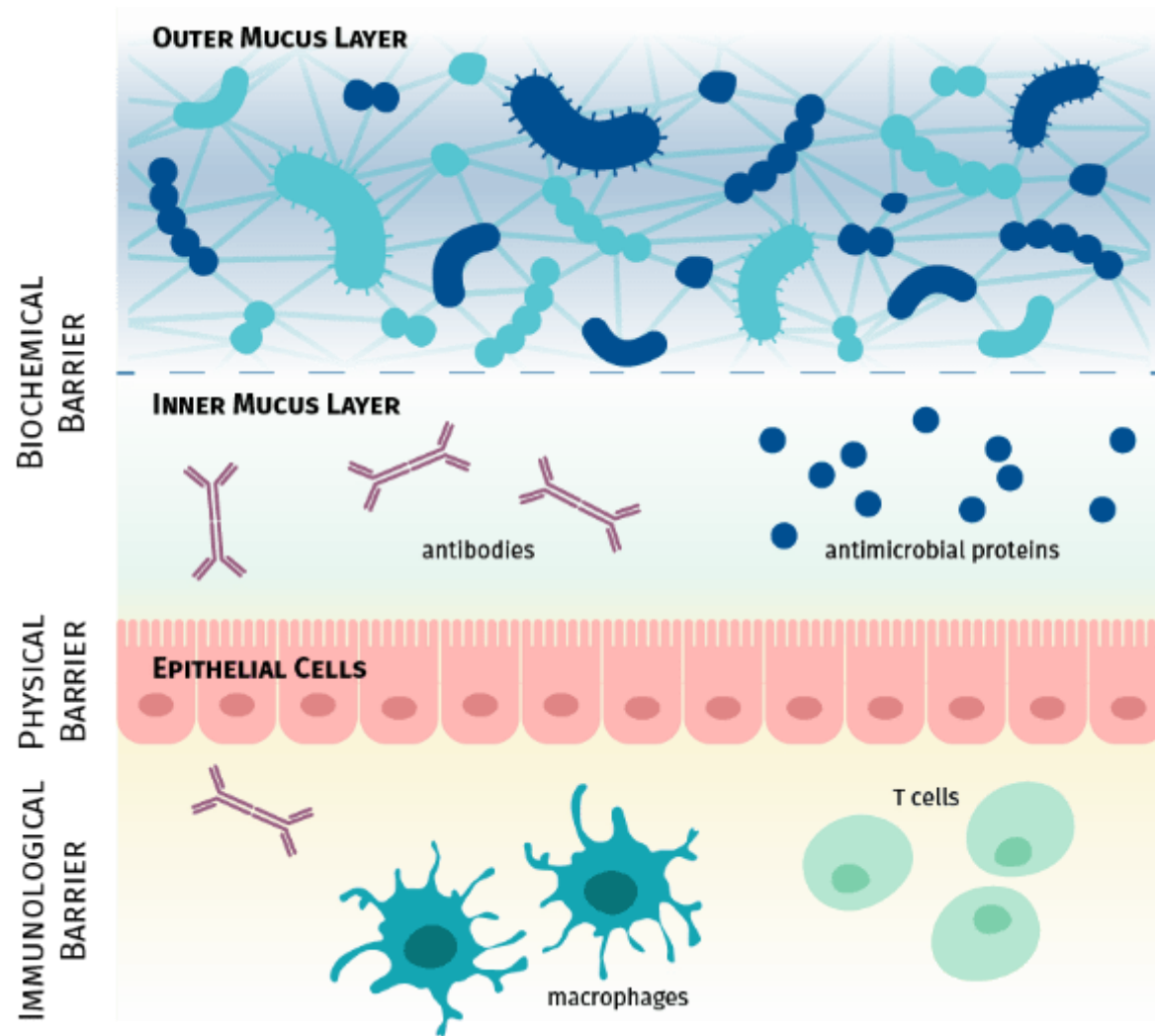
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# A Uniquely-Positioned Microbiome Company



# Host – Microbiota Interactions are Critical for a Functional Immune System



Cross-section of a healthy gut

A rich and diversified gut ecosystem actively modulates the immune system functionality

- A diversified microbiome contributes to the education and modulation of our immune system throughout life
- Bacterial richness and mucus layer prevent colonization by pathogens and improve gut barrier

80%

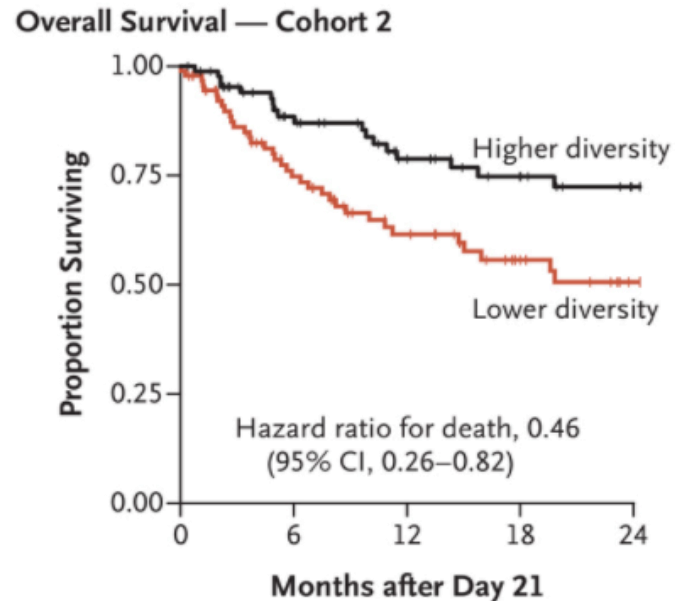
cellular host defense localized in the gut

# Diversity matters!

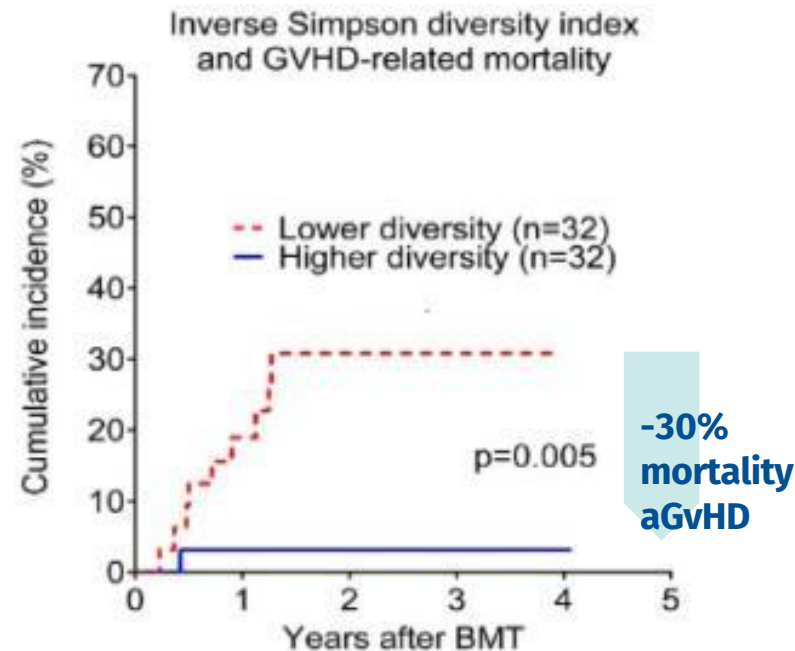
## Higher gut microbiome diversity is associated with ...

### Liquid Tumors

Higher survival rate in patients receiving allo-HSCT <sup>\*,1</sup>



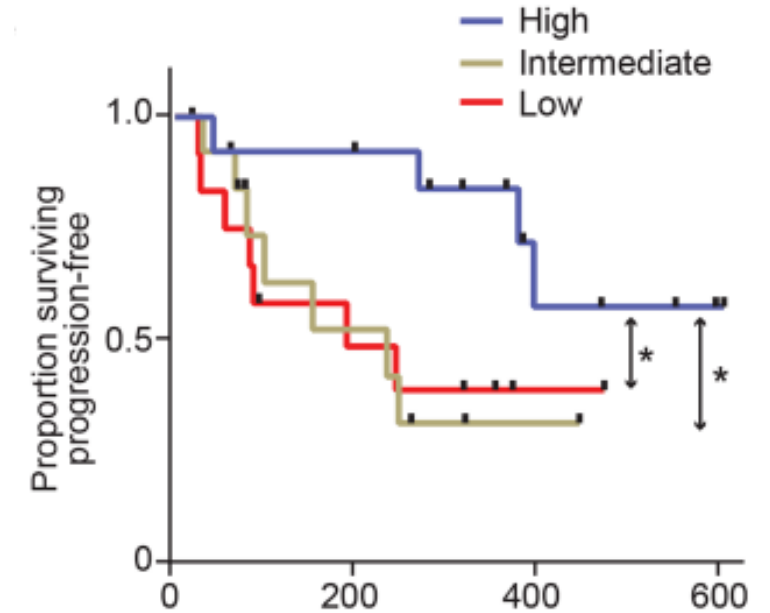
Lower incidence and lower mortality from aGvHD<sup>\*,2</sup>



MaaT Pharma MET Inverse Simpson (mean): 24

### Solid Tumors

Higher response rate to ICI\* in patients with metastatic melanoma<sup>3</sup>



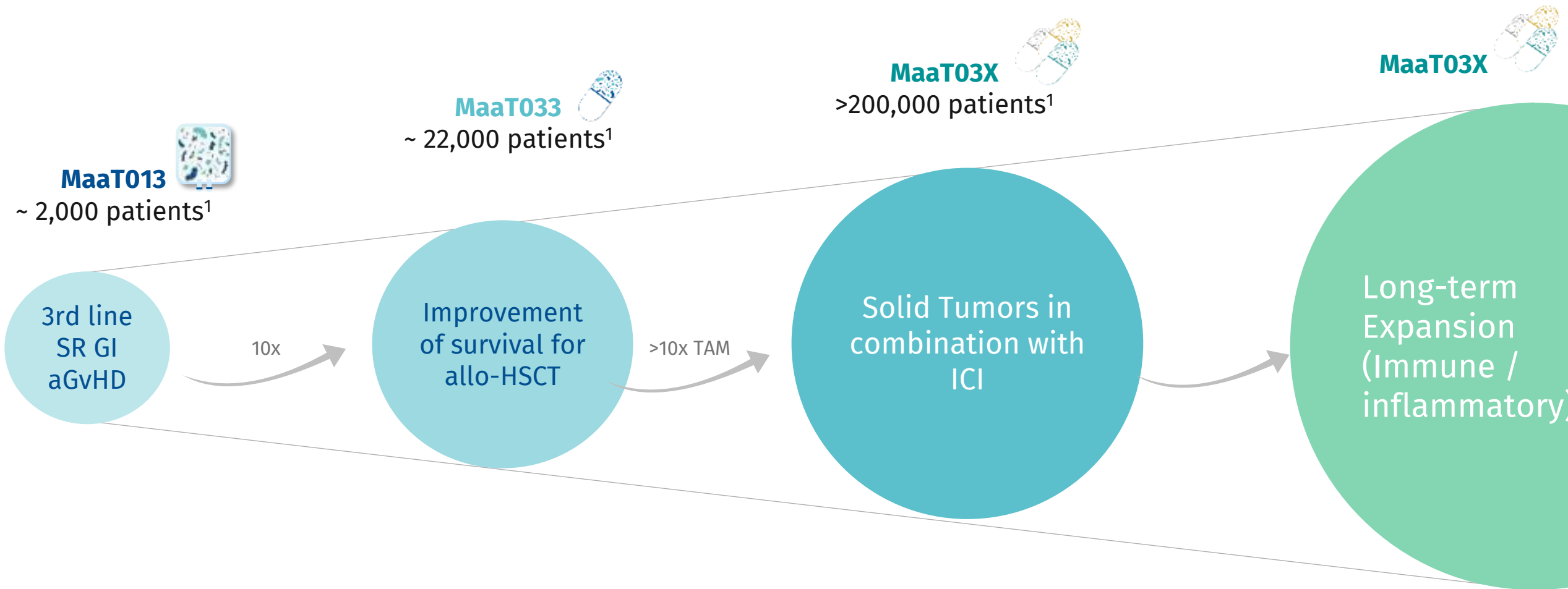
\*allo-HSCT: allogeneic hematopoietic stem cell transplantation; aGvHD: acute Graft-vs-host-Disease; ICI: Immune Checkpoint Inhibitors  
<sup>1</sup>Peled, J.U. & al N Engl J Med 2020;382:822-34; <sup>2</sup>Ghani, 2021; Jenq RR. et al, Biol Blood Marrow Transplant 21 (2015) 1373e1383; Pamer, Blood, 2014; <sup>3</sup>Gopalakrishnan et al., Science, 2017, see also Routy et al, Science, 2018; Vetizou et al Science 2015;

# MaaT Pharma's Microbiome Ecosystem Therapy (MET) platform has generated a diverse line of product candidates

Platform	Program	Indication	Preclinical	Phase I	Phase II	Phase III	Upcoming milestone
MET-N	MaaT013	aGvHD	<b>ARES</b>				DSMB H2 2023
		IO Melanoma	<b>PICASSO (IST)</b>				Results H2 2024
	MaaT033	HSCT	<b>PHOEBUS</b>				Initiation H2 2023
		ALS	<b>IASO</b>				FPI 2023
MET-C	MaaT03X	Multiple	<b>R&amp;D</b>				Targeting FIH 2024

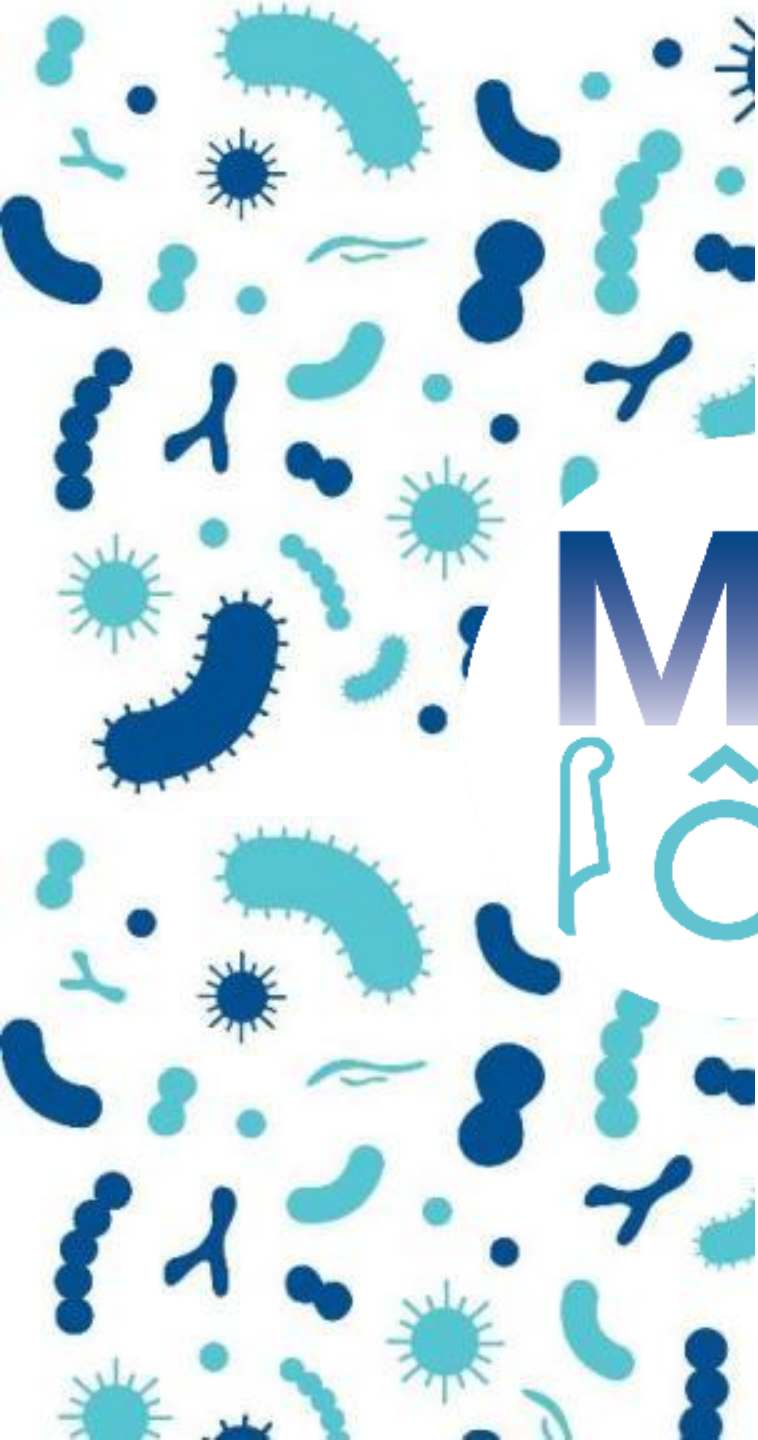
*IST: Investigator Sponsored Trial; aGvHD: acute Graft-versus-Host Disease; IO: Immuno-oncology; HSCT: Hematopoietic Stem Cell Transplantation; ALS: Amyotrophic Lateral Sclerosis*

# Looking ahead: addressing growing market opportunities with severe medical need



<sup>1</sup> EU5, US, and Japan





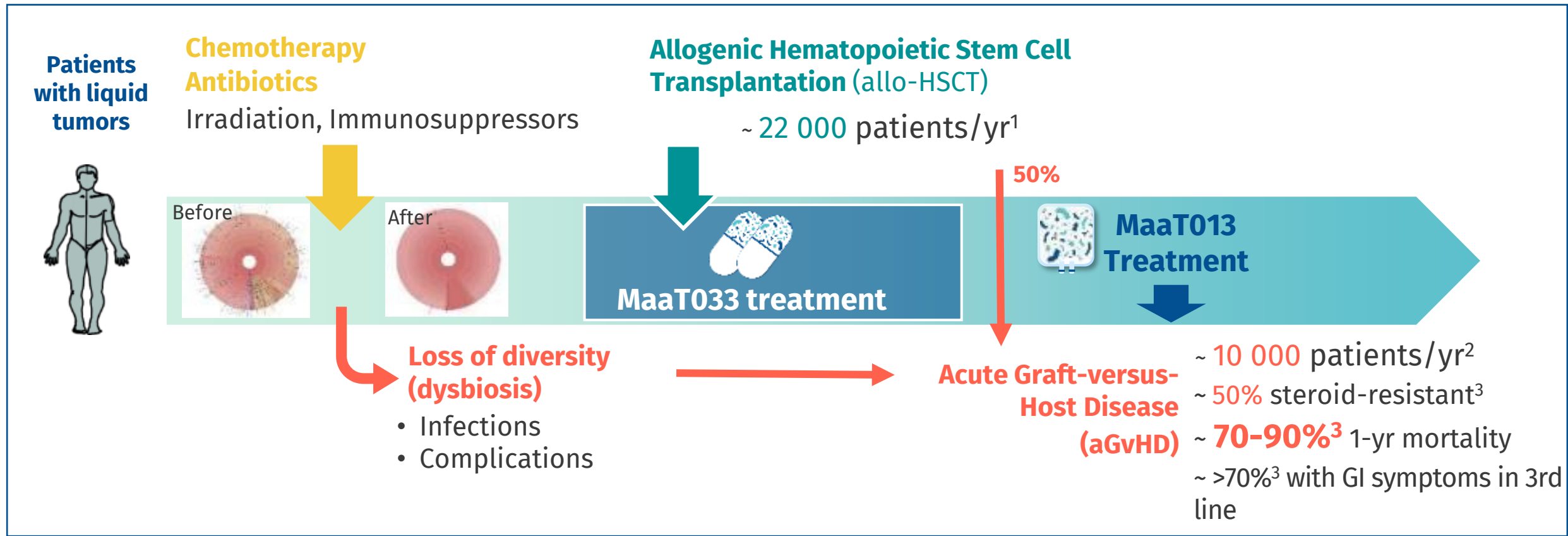
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Hemato-Oncology



# MaaT013 and MaaT033 aim to restore the gut microbiota to improve survival in patients with liquid tumors

Intestinal dysbiosis is associated with higher mortality in hemato-oncology



1. EU5 + US : (~ 20 500 primary procedures with an additional 7%-10% recurring), 2. EU5 + US, <sup>3</sup> According to MAGIC database

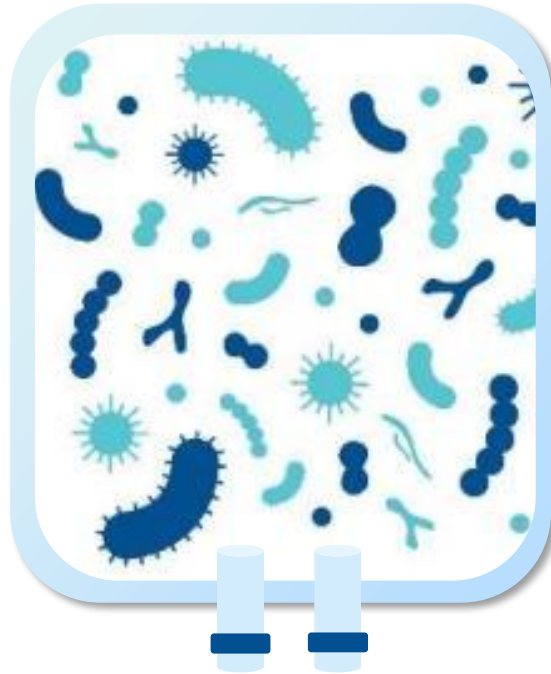


Hemato-Oncology

Treatment of acute Graft-vs-Host-Disease  
(aGvHD)



# MaaT013: restore the microbiome to *cure* gastrointestinal acute Graft vs. Host Disease



Acute, hospital use



## Characteristics

Pooled microbiota: a high-richness, high-diversity, full ecosystem, Microbiome Ecosystem Therapy containing Butycore™



## Administration

3 doses (*enema bag*)



## Available Clinical Data

- ✓ HERACLES Phase 2 Clinical Trial, N=24, 2L
- ✓ Early Access Program, data from N=81, 3L-6L, program still ongoing
- >160 patients treated to date



## Efficacy evaluation (GI ORR at Day28)

Complete response (CR), Very Good Partial Response (VGPR), Partial Response (PR)



## Current indication

Gastrointestinal acute Graft-versus-Host Disease

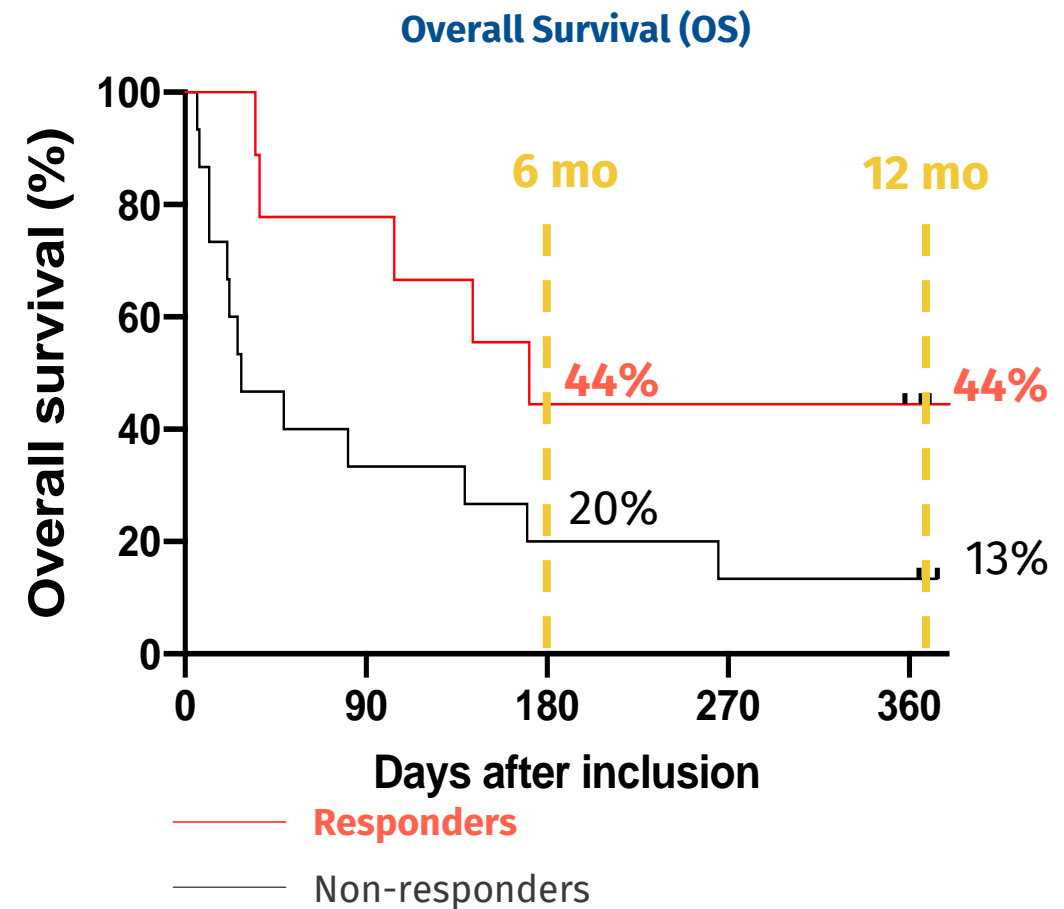
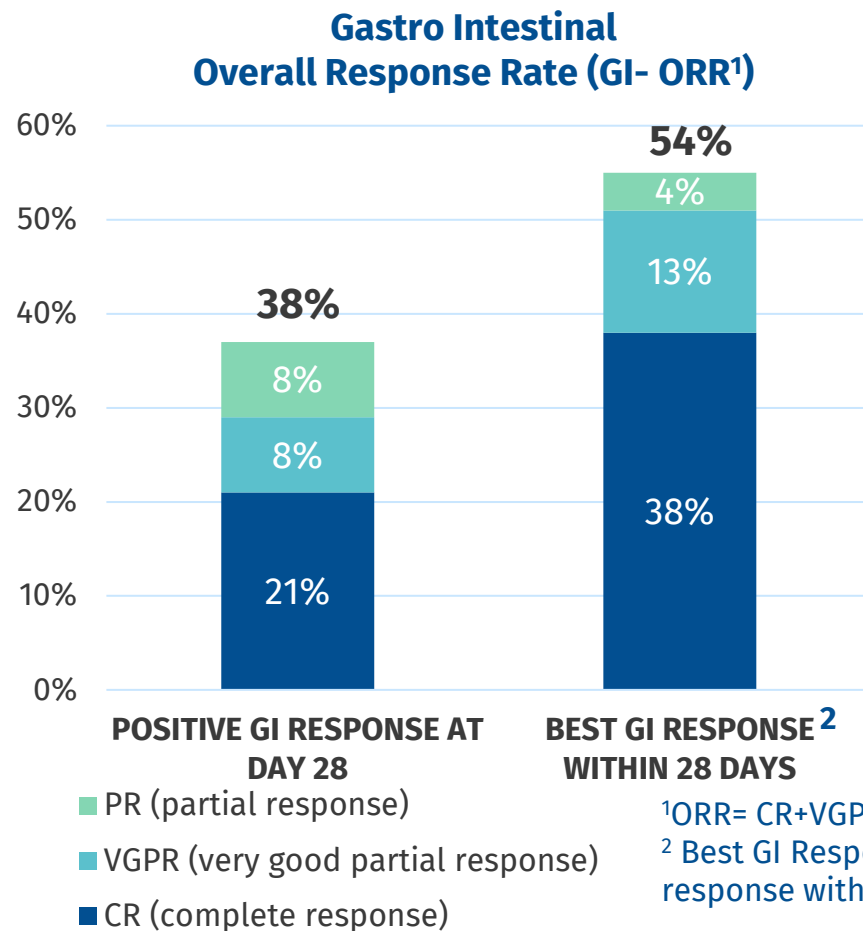
MaaT013 has received Orphan Drug Designation from FDA and EMA



# HERACLES Phase 2 Clinical Trial

## Promising results in a very severe (III-IV) GI aGvHD population

- N=24 patients, 96% grade III (4% grade IV), 2<sup>nd</sup> line (Steroid-resistant)
- Very good safety and tolerability profile
- MaaT013 increases responders' gut microbiome diversity

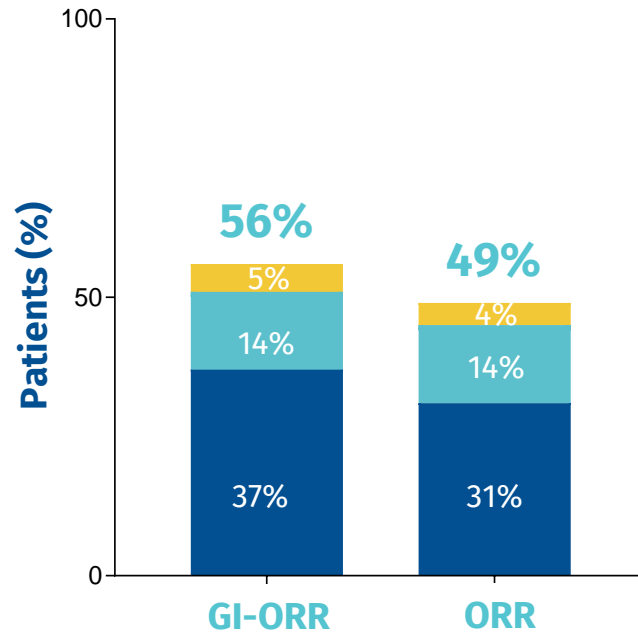




# Early Access Program (EAP) is corroborating positive data in an advanced, severe and more diverse GI aGvHD population

- N=81 84% SR; Grade III (51%) or Grade IV (38%) aGvHD\*, Up to 6 lines of prior treatment (median 2; 66/81 received ruxolitinib)
- Good tolerability and safety profile in a fragile population
- Data presented in December 2022 at the 64<sup>th</sup> Annual Meeting of the American Society of Hematology (ASH)

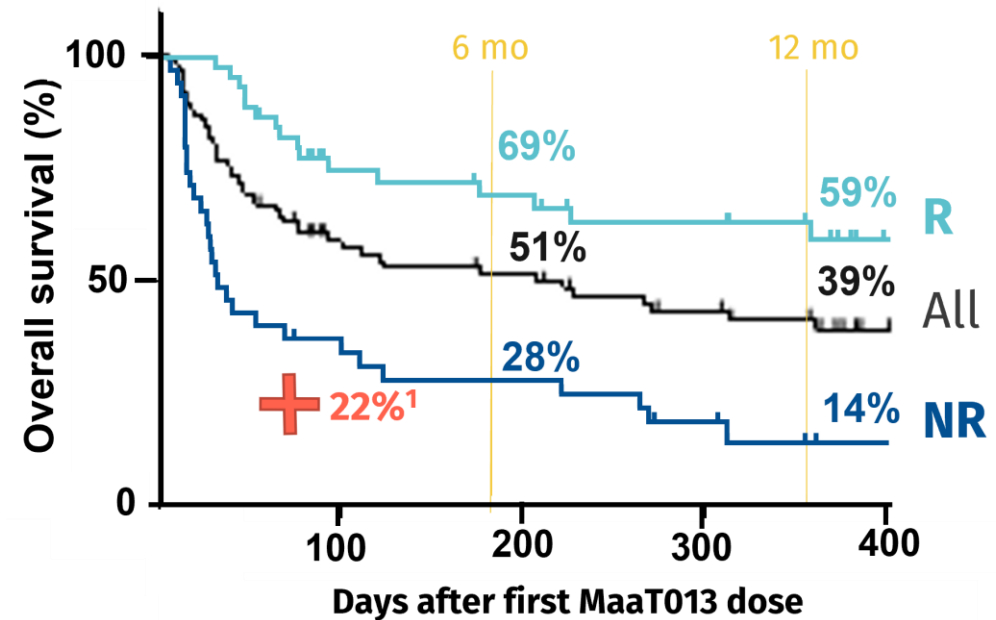
**Gastro Intestinal  
Overall Response Rate (GI- ORR<sup>1</sup>)**



■ CR (Complete Response)  
■ VGPR (Very Good Partial Response)  
■ PR (Partial Response)

<sup>1</sup>ORR= CR+VGPR+PR

**Overall Survival Rate  
Responders vs. Non responders**



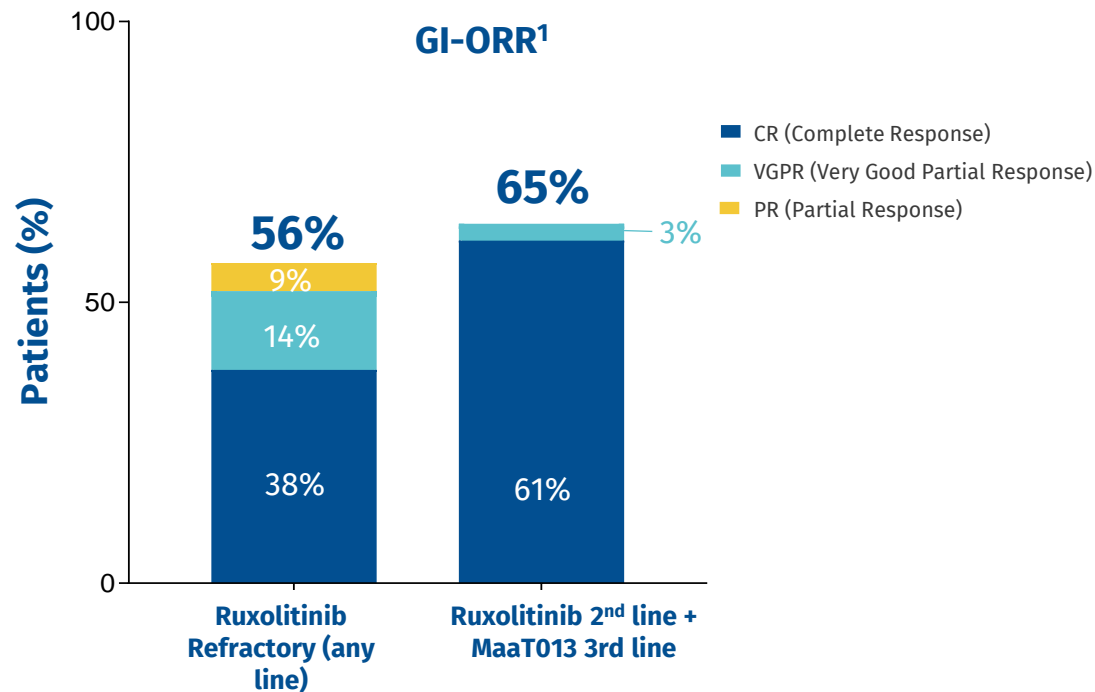
<sup>1</sup>OS expected in ruxolitinib-resistant patients at 2 months (REACH1 study)

\*(MAGIC Classification)



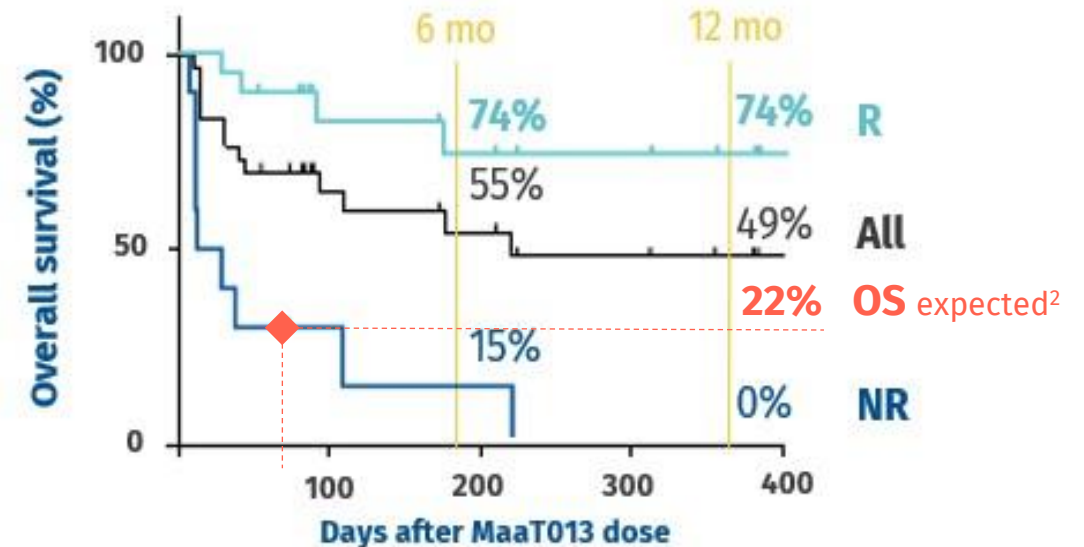
# Among 81 patients in EAP, excellent response to MaaT013 was shown in n=31 corticoid and ruxolitinib-refractory patients

- N=31 - Ruxolitinib-refractory in 2<sup>nd</sup> line, MaaT013 given in 3<sup>rd</sup> line
- Clinical response to MaaT013 translates to an important increased overall survival
- Data presented in December 2022 at the 64<sup>th</sup> Annual Meeting of the American Society of Hematology (ASH)



<sup>1</sup>ORR= CR+VGPR+PR

## Overall Survival Rate in ruxolitinib-refractory patients Responders vs. Non responders



<sup>2</sup>OS at 2 mo in ruxolitinib-resistant patients (REACH1 study)

**This patient population resembles the ongoing Phase 3 ARES clinical trial (NCT04769895) being conducted in Europe.**



# The ARES Phase 3 study is designed to establish MaaT013 as the 3<sup>rd</sup> line agent in GI aGvHD treatment

- Further investigation currently ongoing in a pivotal single arm Phase 3 trial of MaaT013 as 3<sup>rd</sup> line
- 75 patients with GI aGvHD who are refractory to both steroids and ruxolitinib
- Primary endpoint: GI-ORR at Day28

## EUROPE: ongoing clinical trial

- ✓ First patient dosed in Q1 2022
- ✓ CTA approved in 6 European countries: Austria, Belgium, France, Germany, Italy, Spain.

## USA: FDA IND cleared to enable clinical activity in the U.S.

- ✓ Lift of clinical hold in April 2023
- ✓ MaaT Pharma intends to consult with the FDA on the next steps of the regulatory process to bring MaaT013 to US patients in the most expeditious way possible.

### Targeted Timelines ARES Phase 3 Trial



Clinical trials.gov : [NCT04769895](https://clinicaltrials.gov/ct2/show/study/NCT04769895)

ORR: overall response rate ; OS: overall survival ; MAA: Market approval authorization  
Corporate Presentation





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Hemato-Oncology

Improving survival in allogeneic Hematopoietic  
Stem Cell Transplantation patients

# MaaT033: An oral capsule to be used as an *adjunctive therapy* for patients with hematological malignancies receiving HSCT



ambulatory market,  
acute and chronic conditions



## Characteristics

Pooled microbiota: high-richness, high-diversity, full ecosystem, Microbiome Ecosystem Therapy containing Butycore™



## Administration

Oral (a lyophilized capsule)



## Clinical program

- ✓ CIMON P1b: Dose-finding study (completed)
- Planning **P2b trial** to evaluate MaaT033 to improve overall survival in allo-HSCT patients



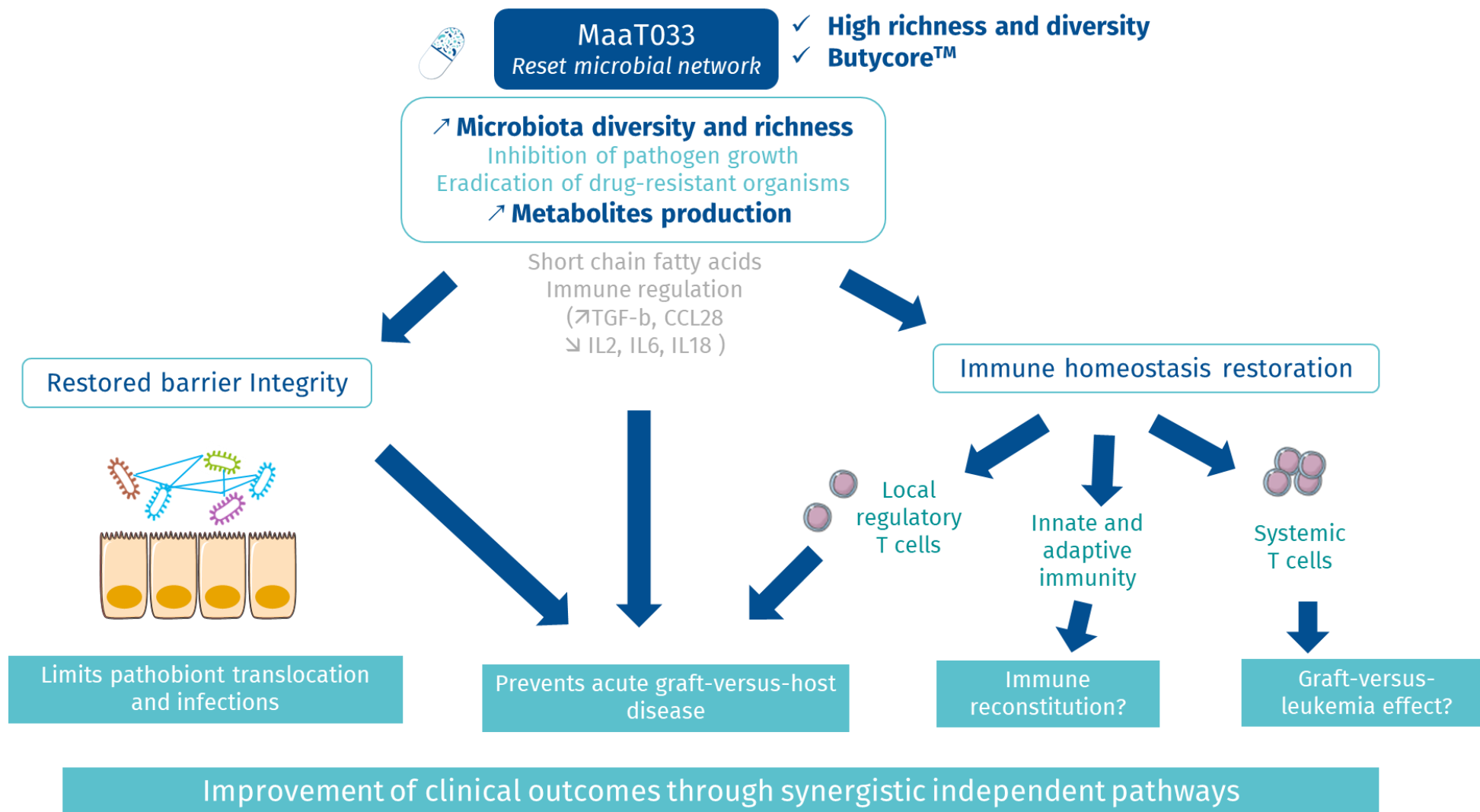
## Indication

To improve overall survival of allo-HSCT patients

MaaT033 has received Orphan Drug Designation from EMA



# MaaT033's MOA aims to *restore and protect* the gut microbiota, to improve overall survival in allo-HSCT patients

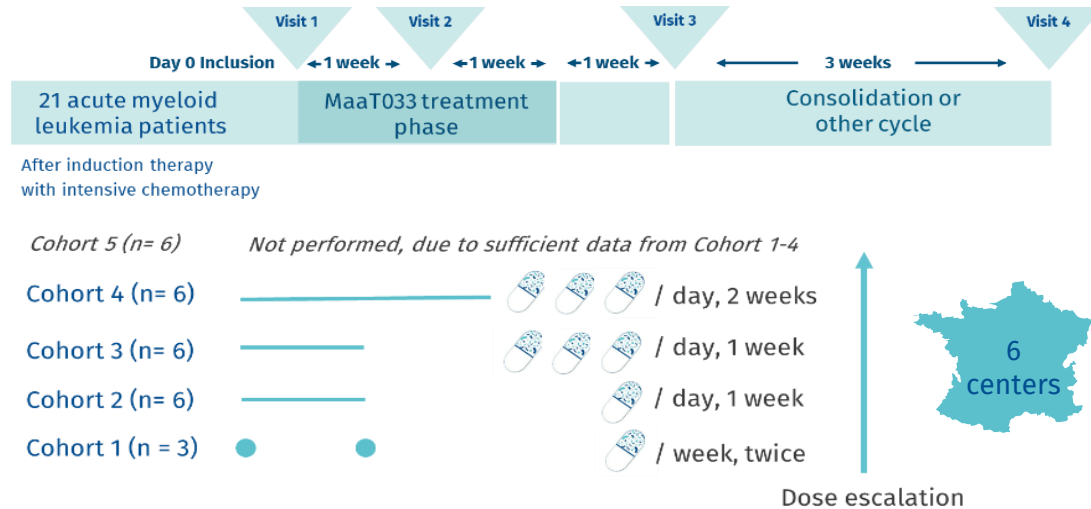




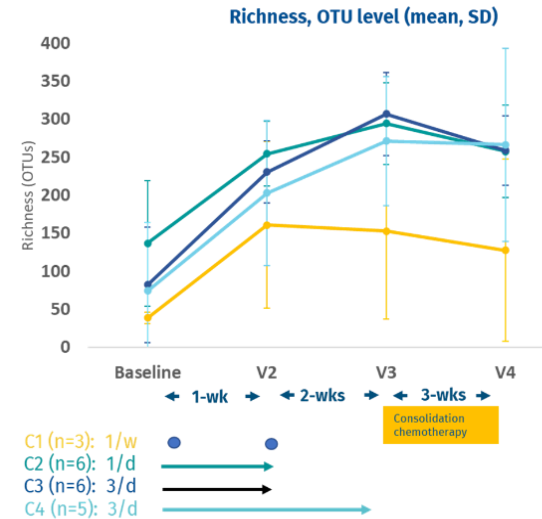
# Phase Ib CIMON study: Positive dose ranging study with promising engraftment and safety data



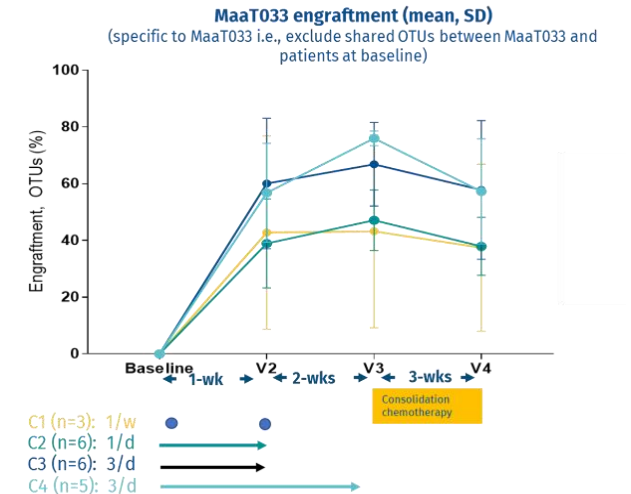
Phase Ib study aimed to determine MaaT033 dose for further clinical development



MaaT033 induces an increased microbiota richness at OTUs level



MaaT033 bacterial engraftment is inversely correlated with patients' baseline microbiota richness



First clinical POC of MaaT033 oral formulation

- ✓ Robust and persistent engraftment
- ✓ Good safety profile:
  - 21 patients exposed, 20 completed.
  - 100% drug compliance.
  - 4/4 positive DSMB meetings
- ✓ Engraftment following MaaT033 treatment correlated with increased anti-inflammatory markers.



# CIMON results open an *attractive market opportunity*: Improving survival in patients receiving allo-HSCT



United States

c. 7,800  
primary  
procedures



EU 5

c. 9,600  
primary  
procedures



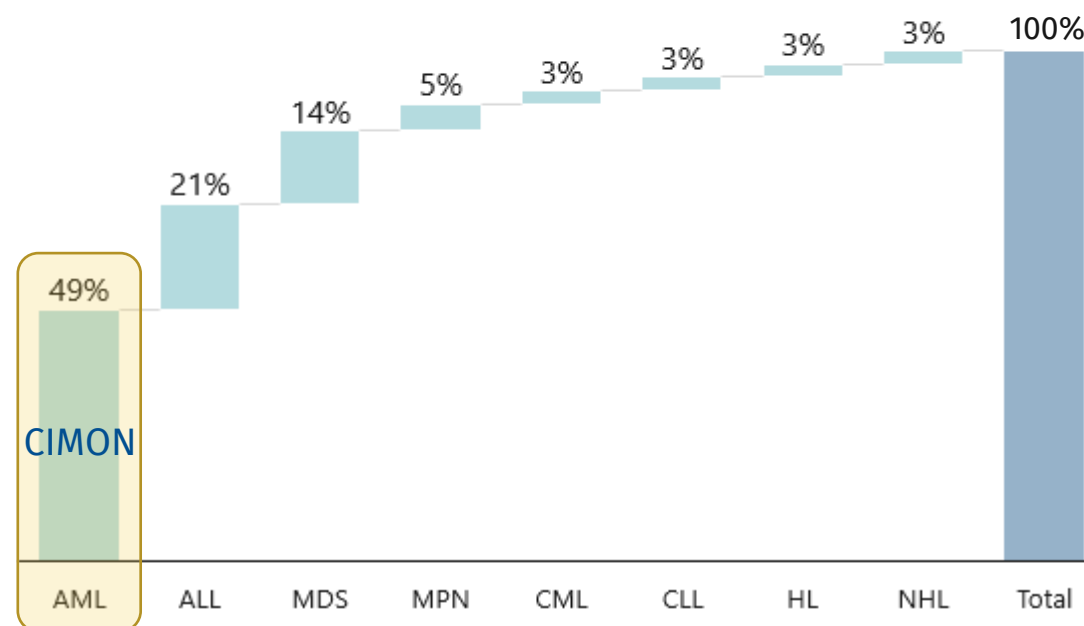
Japan

c. 3,000  
primary  
procedures

Additional 7%-10% recurrent procedures

**Approximately 22,500 procedures/year**

Hematological Malignancy Patients Receiving Allo-HSCT<sup>1</sup>

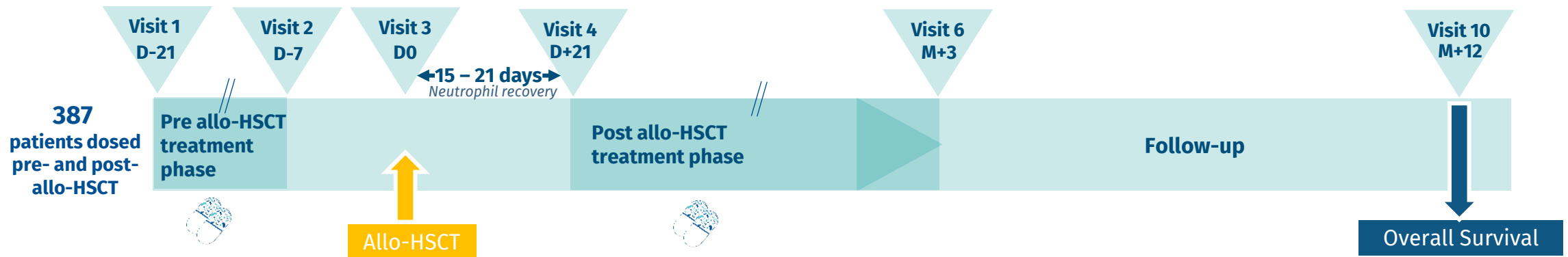


AML : acute myeloid leukemia ; ALL : acute lymphoblastic leukemia ; MDS : myelodysplastic syndrome ; MPN : myeloproliferative neoplasms ; CML: chronic myeloid leukemia ; CLL : chronic lymphocytic leukemia ; HL: Hodgkin's Lymphoma ; NHL: Non Hodgkin Lymphoma

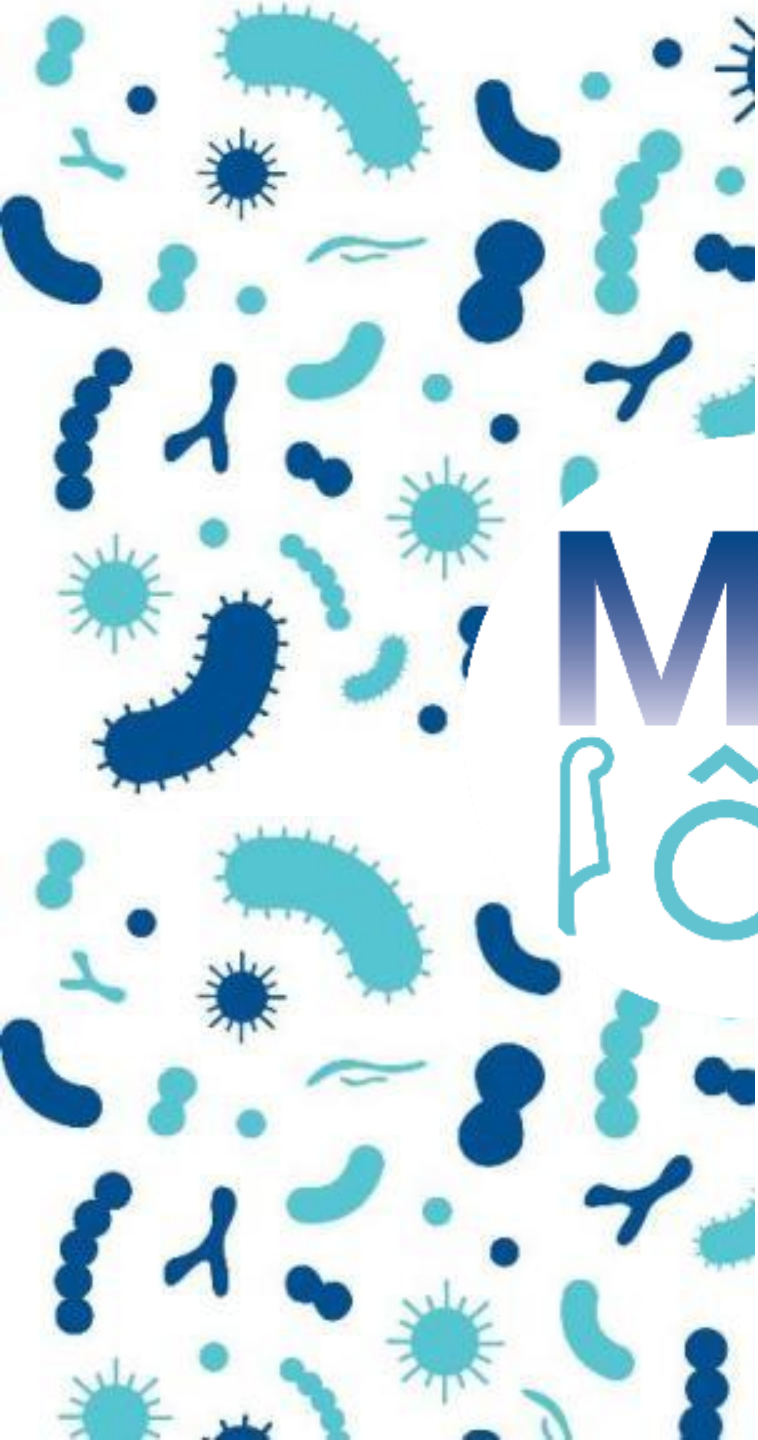
<sup>1</sup>EBMT aHSCT Survey, 2017 (published in Bone Marrow Transplantation (2019) 54:1575–1585), Global Data 2020

# The Phase 2b is designed to establish MaaT033 *as an adjunctive treatment* for patients with hematological malignancies receiving HSCT

- 387 patients in a randomized, double-blind, placebo-controlled international study
- Primary endpoint: efficacy of MaaT033 in improving overall survival at 12 months
- Study is expected to start in H2 2023, results are expected in H1 2026



<sup>1</sup>Expansion to US sites subject to ongoing discussion with the FDA for MaaT013 IND;



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Immuno-Oncology  
Solid Tumors



# A diverse gut microbiome increases survival in patients receiving immune checkpoint inhibitors (ICI)

**FMT from ICI responders to ICI non-responding patients with metastatic melanoma**

✓ **6/15**

Non-responders  
→ Responders  
(Davar et al, 2021)

✓ **3/10**

Non-responders  
→ Responders  
(Baruch et al, 2021)



- Immune check-point inhibitors (ICI) therapies have established themselves as key therapeutic options in solid tumors, but ORR may be as low as 20% in some indications.
- Richness, Diversity and composition of gut microbiome drive survival and ICI toxicity in patients receiving ICI<sup>1,2,3,4</sup>
- FMT from ICI responders (R) could induce response in metastatic melanoma non-responders (NR)<sup>5,6</sup>

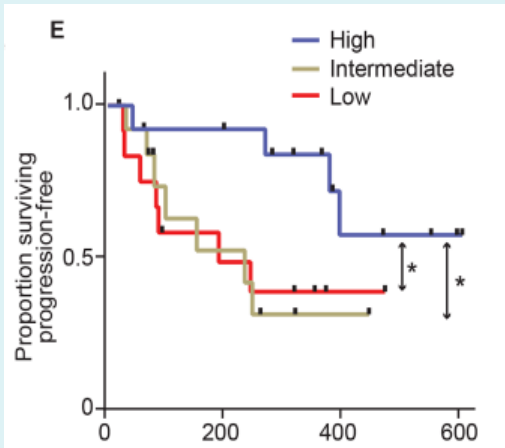
→ Leveraging the gut microbiome richness, diversity and its key functional networks may be a game-changer in immunology in the coming years

<sup>1</sup>. Gopalakrishnan et al, Science 2018, <sup>2</sup>. Matson, et al Science 2018; <sup>3</sup>. Routy et al, Science 2017;

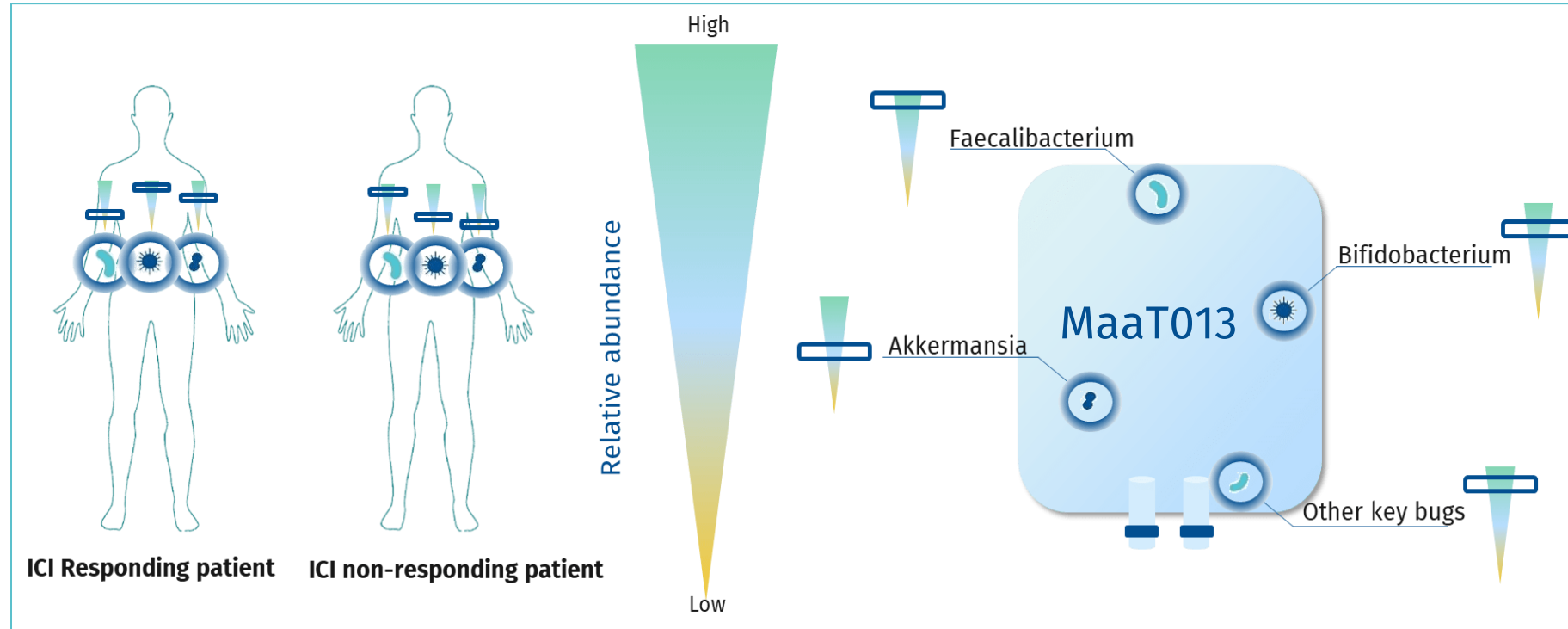
<sup>4</sup>. Mc Culloch et al, Nat Med 2022; <sup>5</sup>. Baruch et al, Science 2021; <sup>6</sup>. Davar et al, Science 2021

# MaaT013 ensures high diversity and contains specific bacterial strains that have been identified to improve ICI response

Higher microbiome richness → better response rate to ICI in patients with metastatic melanoma



Gopalakrishnan et al, Science 2018

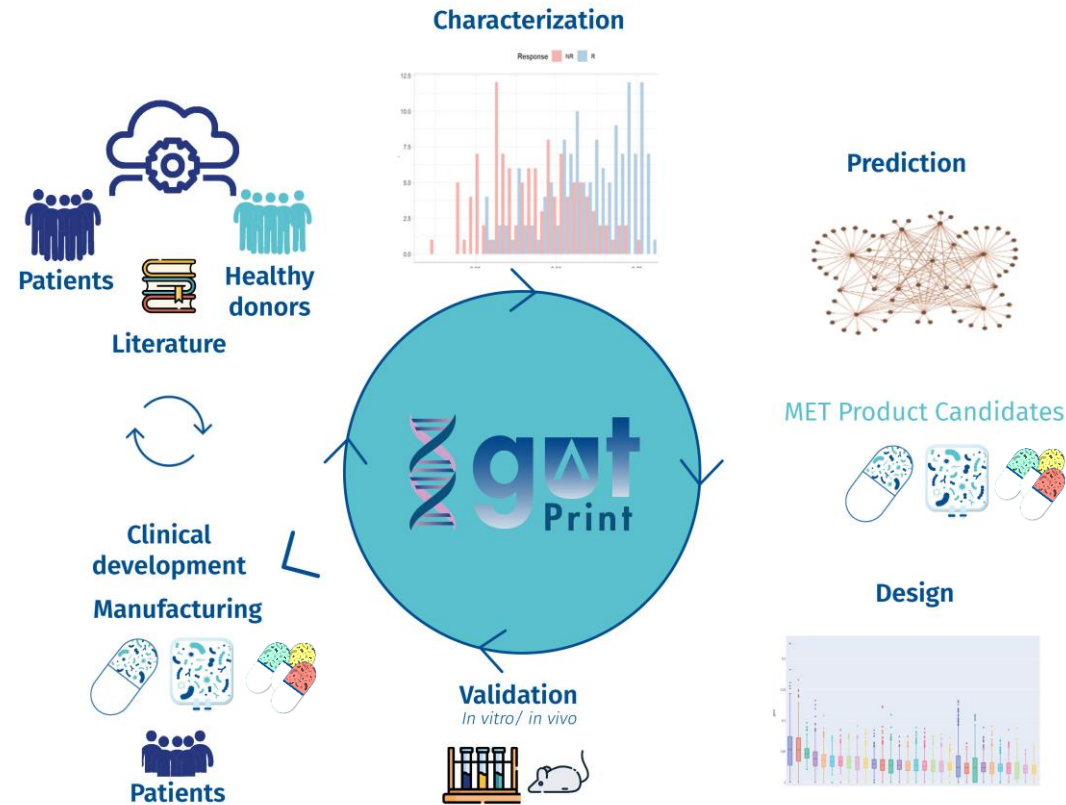


**Ongoing Phase IIa PICASSO trial<sup>1</sup>**, in collaboration with **Assistance Publique - Hôpitaux de Paris** (sponsor).

- ✓ **RCT** [MaaT013 + ICI] vs. [Placebo + ICI] in **60** metastatic melanoma patients
- ✓ **Key study endpoints** after 23 weeks of treatment:
  - MaaT013 safety profile vs placebo as add-on treatment to Ipilimumab + Nivolumab
  - MaaT013 best-overall response rate vs placebo as add-on treatment to Ipilimumab + Nivolumab

<sup>1</sup> Registered trial #NCT04988841

# Proprietary gutPrint® platform synergizes multi-source data to generate innovative and indication-specific microbiome ecosystem therapies



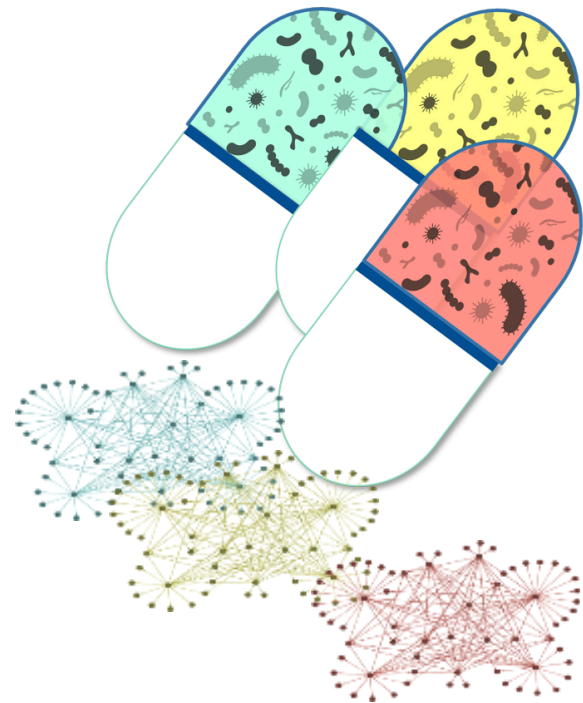
gutPrint® is the engine that drives MaaT Pharma's MET product candidate generation capabilities to broaden and strengthen the pipeline

- ✓ Full cycle in 15 months to enter clinical phase

# MaaT03X: Modulate the gut microbiome to *improve response* to Immune Checkpoint Inhibitors treatment in solid tumors



MaaT03X  
I/O



## Characteristics

High richness, co-cultured,  
designed ecosystem



## Administration

Oral (proprietary lyophilized capsule)



## Development program

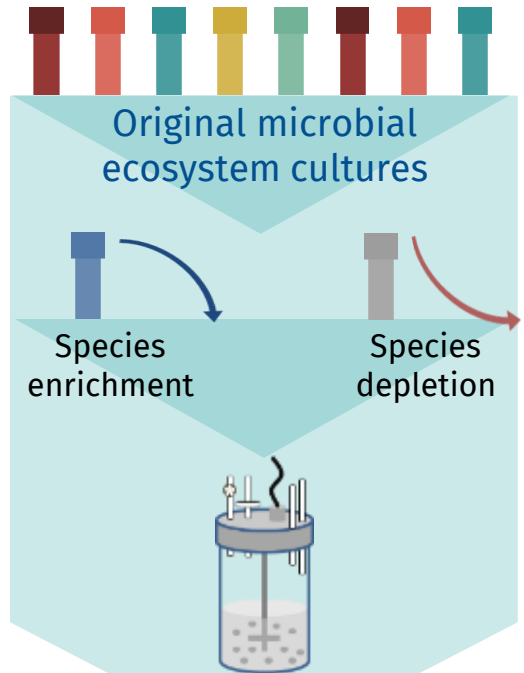
- ✓ First candidate in preclinical development
- Targeting FIH H1 2024



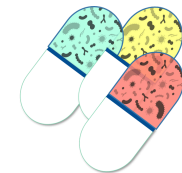
## Indication

Improvement of response to ICI  
Potential to be declined to multiple indications

## Customizable, donor-independent, scalable co-culture process



CO-CULTURED A FULL ECOSYSTEM



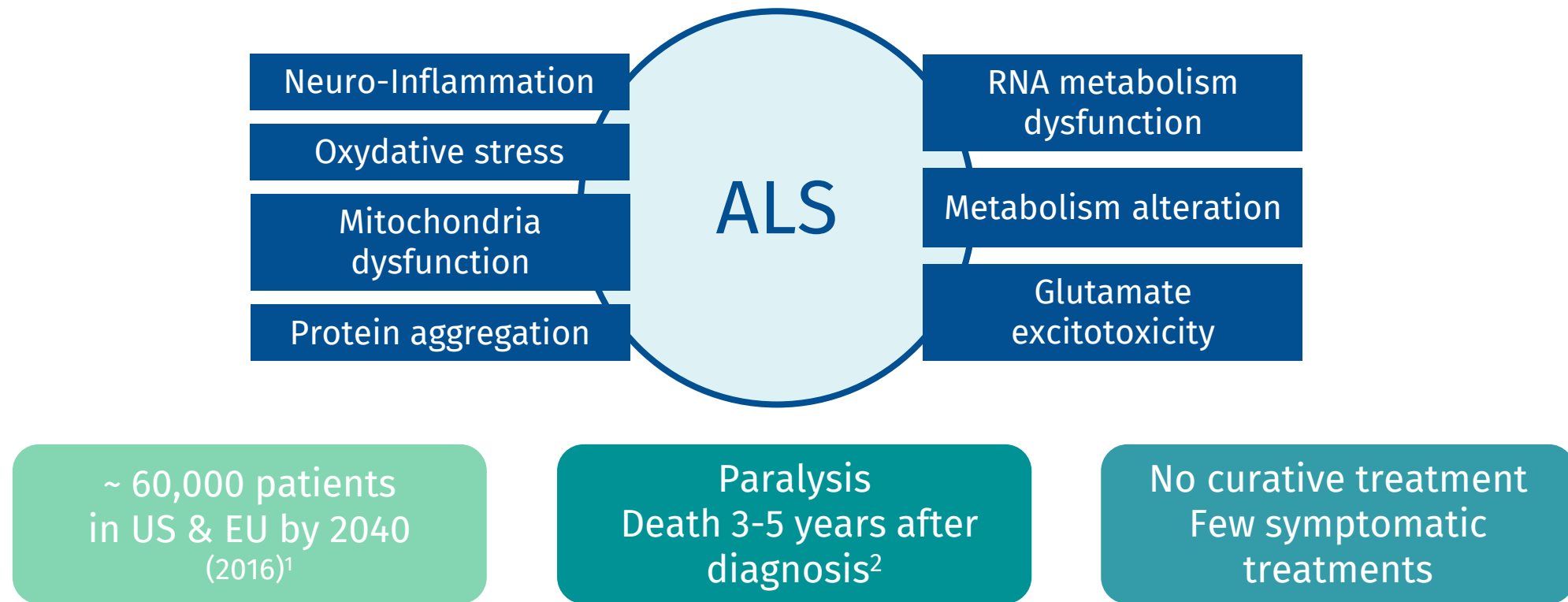


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Neuro-degenerative diseases:  
Amyotrophic Lateral Sclerosis  
(ALS)



# Amyotrophic Lateral Sclerosis: a incurable disease leading to death within 3-5 years after diagnosis



<sup>1</sup>Arthur, K., Calvo, A., Price, T. et al. Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. *Nat Commun* 7, 12408 (2016). <https://doi.org/10.1038/ncomms12408>

<sup>2</sup><https://tousensellescontrelasla.fr/la-sla-cest-quoi/>





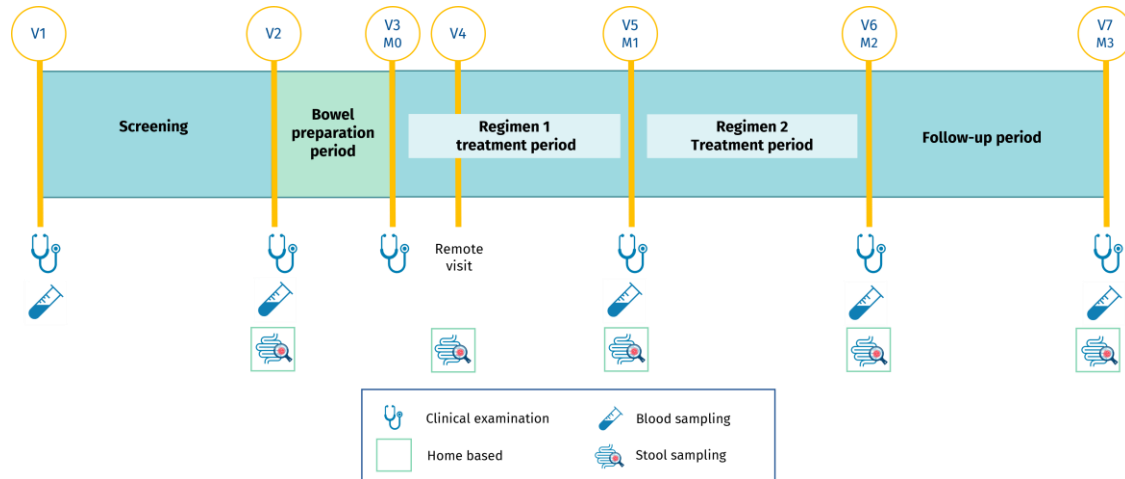
# IASO trial is designed to develop the potential first oral microbiotherapy in ALS\*

- Up to 15 patients in a pilot, open-label, Phase 1b study in France
- Study is expected to start in 2023, results are expected in H1 2024

Study developed with:



With the support of



## Key study endpoints:

- Assess safety and tolerability of multiple doses of MaaT033
- Assess gut microbiota composition evolution
- Identify biomarkers sensitive to treatment before considering a larger randomized controlled efficacy study

Potential to extend further to other chronic CNS diseases/ immuno-inflammatory diseases as MaaT Pharma collects data and in-depth understanding of MOA.

\* One academic study testing native gut microbiome in ALS patients using **an invasive administration** procedure on going.





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End-to-End in-house cGMP  
manufacturing

# Building Europe's largest specialized cGMP manufacturing facility for Microbiome Ecosystem Therapies



Building a dedicated 1,600m<sup>2</sup> site (which could be doubled) to support up to 2034 needs of clinical and then commercial production of native MET (MaaT013 & MaaT033) and R&D and clinical batches of cultured products MaaT03X (est. first step):



MaaT013



9,000 per year



MaaT033



1 300 000 capsules per year



MaaT03X



Up to 300,000 capsules per year



Site provides for a fully integrated Manufacturing and development platform to allow for a quick and efficient product development, scaleup and GMP process.

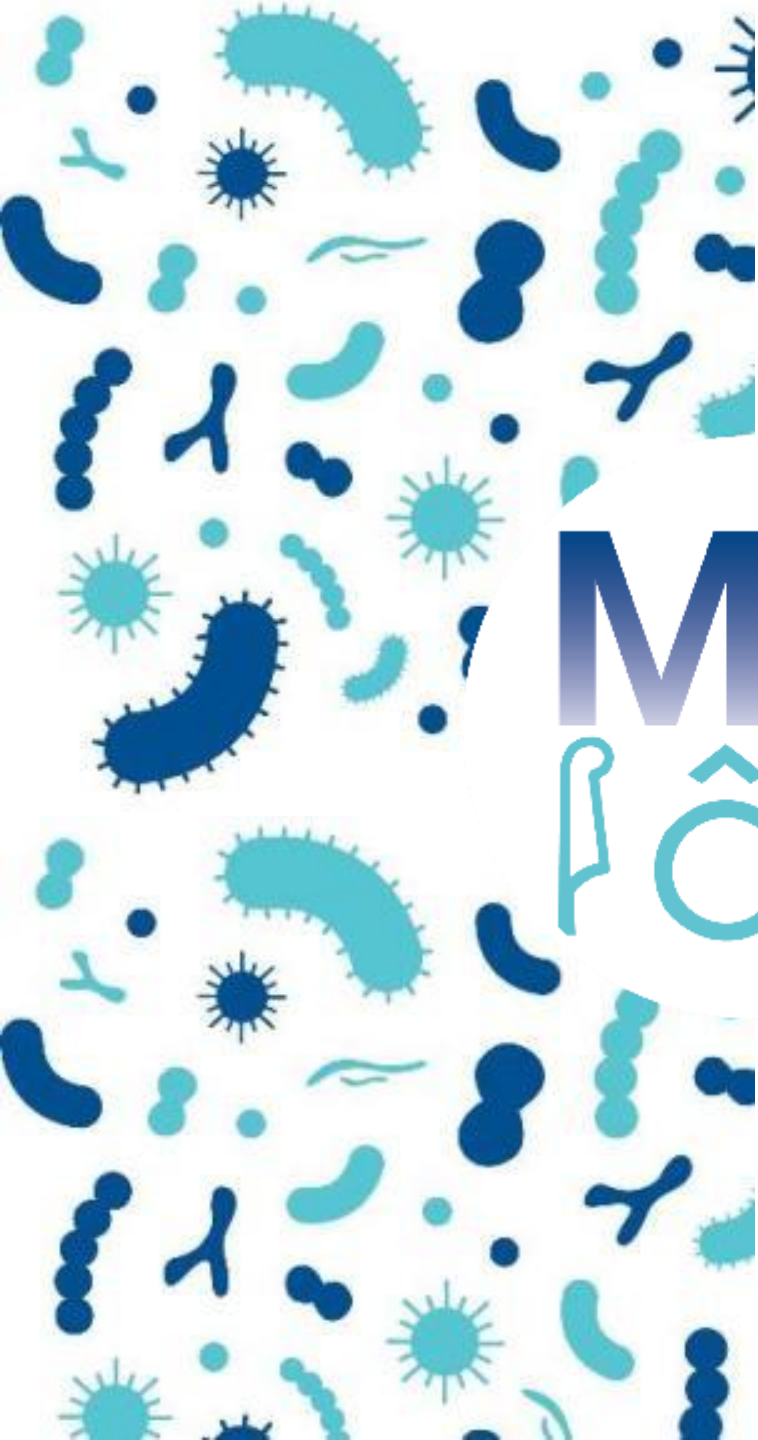


Ongoing CSR global strategy: participating in a reforestation program in France (opting for more ecological items (GoGreen) and joining the Cap Vert pour la forêt program and furnishing the plant with sustainable & used materials

Partnership with  Skyepharma



Production campaign targeted to start  
by the end of Q3 2023



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Upcoming key milestones

# Meaningful milestones in both the near and long term

2023	2024	2025/2026+
<div><b>MaaT013 (pooled enema)</b><ul style="list-style-type: none"><li>GvHD   ARES P3 DSMB H2</li><li>IO in Melanoma   PICASSO P2a Internal Review</li></ul></div> <div><b>MaaT033 (pooled capsule)</b><ul style="list-style-type: none"><li>HSCT   PHOEBUS P2b Launch H2</li><li>ALS   IASO P1b FPI</li></ul></div>	<div><b>MaaT013 (pooled enema)</b><ul style="list-style-type: none"><li>GvHD   ARES P3 ORR mid-year</li><li>IO in Melanoma   PICASSO P2a Results H2</li></ul></div> <div><b>MaaT033 (pooled capsule)</b><ul style="list-style-type: none"><li>HSCT   PHOEBUS P2b Safety Interim H2</li><li>ALS   IASO P1b Results H2</li></ul></div> <div><b>MaaT03X (co-cultured capsule)</b><ul style="list-style-type: none"><li>Undisclosed   Targeting FIH</li></ul></div>	<div><b>MaaT013 (pooled enema)</b><ul style="list-style-type: none"><li>GvHD   Final Results (OS)</li><li>GvHD   Commercial launch</li></ul></div> <div><b>MaaT033 (pooled capsule)</b><ul style="list-style-type: none"><li>HSCT   PHOEBUS Results</li></ul></div> <div><b>MaaT03X (co-cultured capsule)</b><ul style="list-style-type: none"><li>Undisclosed   P1b Results</li></ul></div>

# Key differentiators of MaaT Pharma from other microbiome competitors

## Leveraging the complexity of the microbiome

Pioneering a **full ecosystem approach** to restore host/microbiome **immune symbiosis**, based on proprietary **AI** and manufacturing capacities

## Manufacturing versatility

**In-house cGMP manufacturing** scalability for both native and co-cultured products and end-to-end control of its supply chain

MaaT

## Oncology focus

Addressing **high unmet needs** in the hemato-oncology and immuno-oncology therapeutic areas

## Established proof of concept

**First company to reach Phase 3 testing** for a microbiome product in oncology globally



# A highly experienced team



**Hervé Affagard**

Founder & CEO



**Carole Schwintner, Ph.D**

Chief Technology Officer



**Pr. Gervais Tougas**

Chief Medical Officer



**Siân Crouzet**

Chief Financial Officer



**Philippe Moyen, Ph.D**

Chief Operating Officer



**Nathalie Corvaia, Ph.D**

Chief Scientific Officer



## BOARD OF DIRECTORS



**Karim Dabbagh \***

Chairman of the Board  
President – CEO Second Genome



**Nadia Kamal \***

Non-Executive Director  
Director of the Technology, Health, and Innovation Divisions – Harmonie Mutuelle



**Jean-Marie Lefèvre**

Non-Executive Director  
President – Biocodex



**Isabelle de Crémoux**

Non-Executive Director  
CEO & Managing Partner – Seventure



**Claude Bertrand \***

Non-Executive Director  
General Director R&D – Servier



**Jean Volatier \***

Non-Executive Director  
CFO – Inventiva



**Dorothée Burkel \***

Non-Executive Director  
Former Chief Corporate and People Operations Officer – PartnerRe



**Muriel Prudent**

Censor  
VC Investment Manager – Fonds PSIM – Bpifrance



**Hervé Affagard**

Executive Director  
MaaT Pharma

\* Independent member

# Corporate Social Responsibility

MaaT Pharma aims to become the source of Microbiome excellence providing patients with safe and innovative medicines. The Company develops products from sustainable biological matters, driving optimal impact of Microbiome.

Patients are our priority. We are committed to our patients and to the protection of human health by respecting environmental protection, respecting our employees and ensuring good governance practices. Our way of working every day is driven by the 4 guidelines below:

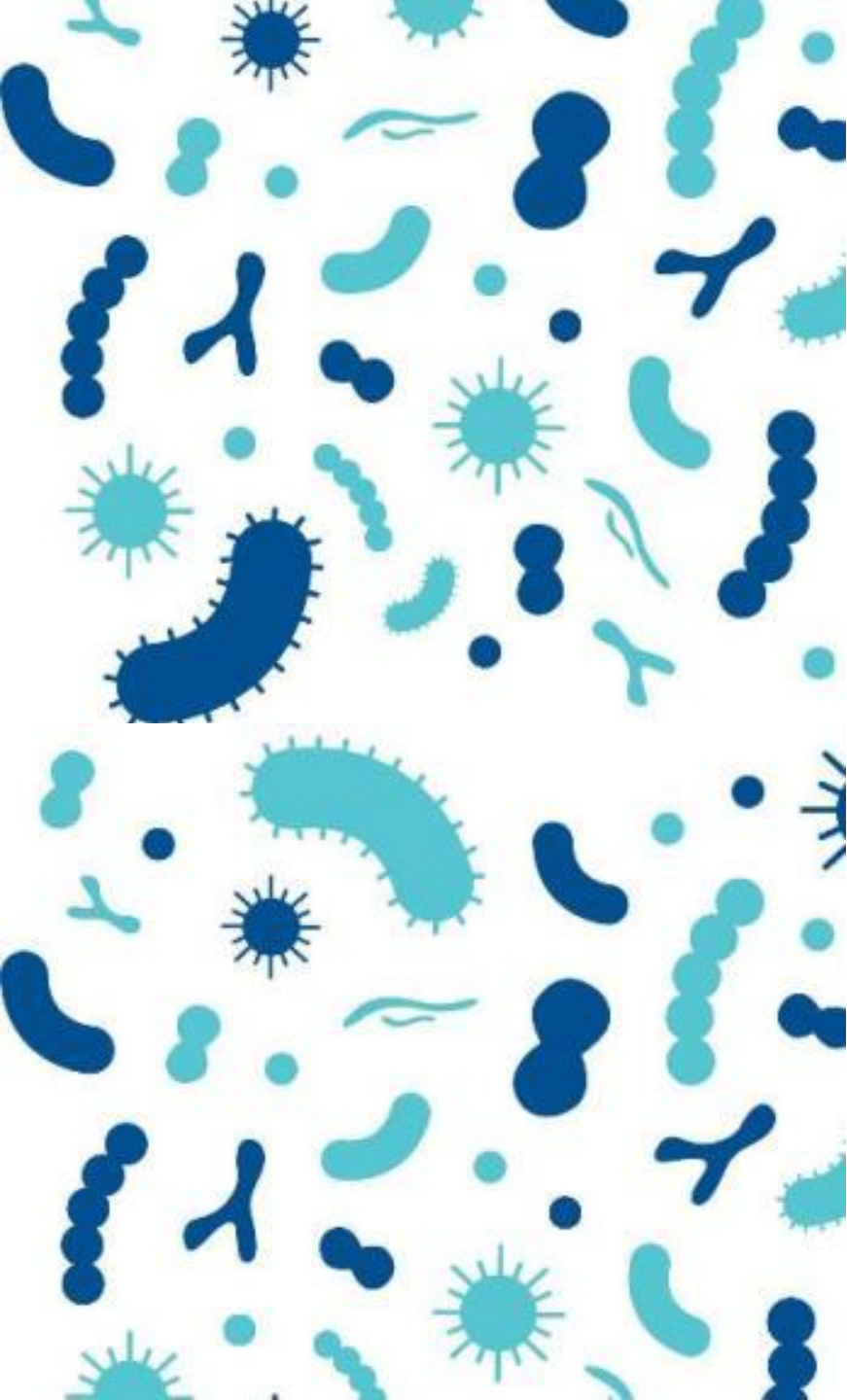
- Innovate and raise awareness to deliver better care,
- Contribute to employees-growth within a people-oriented ecosystem,
- Place ethics and transparency at the core of the Company’s strategy,
- Control and measure our impact on the environment.



## 2022 CSR indicators

SOCIAL	Gender Equality Index	ENVIRONMENT	Carbon footprint	SOCIETAL	Responsibility to patients and practitioners	GOVERNANCE	% of women in the board of directors and management team
	Employment of young people (under 30 and less than 5 years experience)		Energy consumption per employees on site		Increase awareness of Microbiome therapies		% of women in the top 10 earners
	QWL: Job satisfaction				R&D at the focus of our investments		





# THANK YOU

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