

# Enhancing Survival through Microbiome Innovation

July 2024

# Disclaimer

This document has been prepared by MaaT Pharma (the "Company") and is for information and background purposes only.

While the information contained herein has been prepared in good faith, neither the Company, nor its shareholders, directors, officers, agents, employees, or advisors give, have given or have authority to give, any representations or warranties (express or implied) as to, or in relation to, the fairness, accuracy, reliability or completeness of the information in this document, or any revision thereof, or of any other written or oral information made or to be made available to any interested party or its advisers, including financial information (all such information being referred to as "Information"), and liability therefor is expressly disclaimed. Accordingly, neither the Company nor any of its shareholders, directors, officers, agents, employees, affiliates, representatives or advisers take any responsibility for, or will accept any liability whether direct or indirect express or implied, contractual, tortuous, statutory or otherwise, in respect of the accuracy or completeness of the Information or for any of the opinions contained herein or for any errors, omissions or misstatements or for any loss, howsoever arising from this document.

The information and opinions contained in this document are provided as of the date of this document only and may be updated, supplemented, revised, verified or amended, and thus such information may be subject to significant changes. The Company is not under any obligation to update the information or opinions contained herein which are subject to change without prior notice.

The information contained in this document has not been subject to independent verification and are qualified in their entirety by the business, financial and other information that the Company is required to publish in accordance with the rules, regulations and practices applicable to companies listed on the regulated market of Euronext in Paris, including in particular the risk factors and other information in the Company's Document d'enregistrement (Registration Document) registered by the French Autorité des marchés financiers (Financial Markets Authority) (the "AMF") on October 1st, 2021 under no. I.21-0057 and its supplement on October 14, 2021 under no. I.21-0061 and in any other periodic report, which are available free of charge on the websites of the Company (<https://www.maatpharma.com/>) and the AMF ([www.amf-france.org](http://www.amf-france.org)).

No representation, warranty or undertaking, express or implied, is made as to the accuracy, completeness or appropriateness of the information and opinions contained in this document. The Company, its subsidiaries, its advisors and representatives accept no responsibility for and shall not be held liable for any loss or damage that may arise from the use of this document or the information or opinions contained herein.

This document contains information on the Company's markets and competitive position, and more specifically, on the size of its markets. This information has been drawn from various sources or from the Company's own estimates which may not be accurate and thus no reliance should be placed on such information. Any prospective investors must make their own investigation and assessments and consult with their own advisers concerning any evaluation of the Company and its prospects, and this document, or any part of it, may not form the basis of or be relied on in connection with any investment decision.

This document contains certain forward-looking statements. These statements are not guarantees of the Company's future performance. These forward-looking statements relate to the Company's future prospects, developments and marketing strategy and are based on analyses of earnings forecasts and estimates of amounts not yet determinable.

Forward-looking statements are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future. Forward-looking statements cannot, under any circumstance, be construed as a guarantee of the Company's future performance and the Company's actual financial position, results and cash flow, as well as the trends in the sector in which the Company operates, may differ materially from those proposed or reflected in the forward-looking statements contained in this document. Even if the Company's financial position, results, cash-flows and developments in the sector in which the Company operates were to conform to the forward-looking statements contained in this document, such results or developments cannot be construed as a reliable indication of the Company's future results or developments. The Company does not undertake any obligation to update or to confirm projections or estimates made by analysts or to make public any correction to any prospective information in order to reflect an event or circumstance that may occur after the date of this document.

**All persons accessing this document are deemed to agree to all the limitations and restrictions set out above.**

# Late-Stage Clinical Biotech, Leading the Way in Microbiome Therapies in Oncology



## MaaT013 in Phase 3 in aGvHD

- Lead asset MaaT013 in **Phase 3 in aGvHD in Europe, expecting primary endpoint readout in mid Q4**
- **Strong data from Early Access Program** published in April (1y OS 49% vs 15% historical data)
- **US IND Open** – Readiness Phase before launch ongoing



## Deep oncology pipeline

- **Donor-derived** and **co-culture** platforms **driving candidate development** with **2 clinical** and 1 preclinical assets
- **Our gutPrint® AI**, linked to our **co-culture platform**, is poised to deliver, potentially, **clinical-ready candidates by 2025**
- **Largest European cGMP** production facilities for Microbiome Ecosystem Therapies



## Finance



- **Revenues of MaaT013 in aGvHD of 2.2m€ for 2023** from Early Access Program
- **Cash position of 18.2m€** as of March 31, 2024. **Post follow-on in May 2024, (approx. €17.3m€) cash runway** extends into **early Q1/2025**
- **Exploring options to extend cash runway**, including non-dilutive and dilutive sources

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

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



01

A **diversified microbiome** contributes to the **education and modulation of our immune system** throughout life

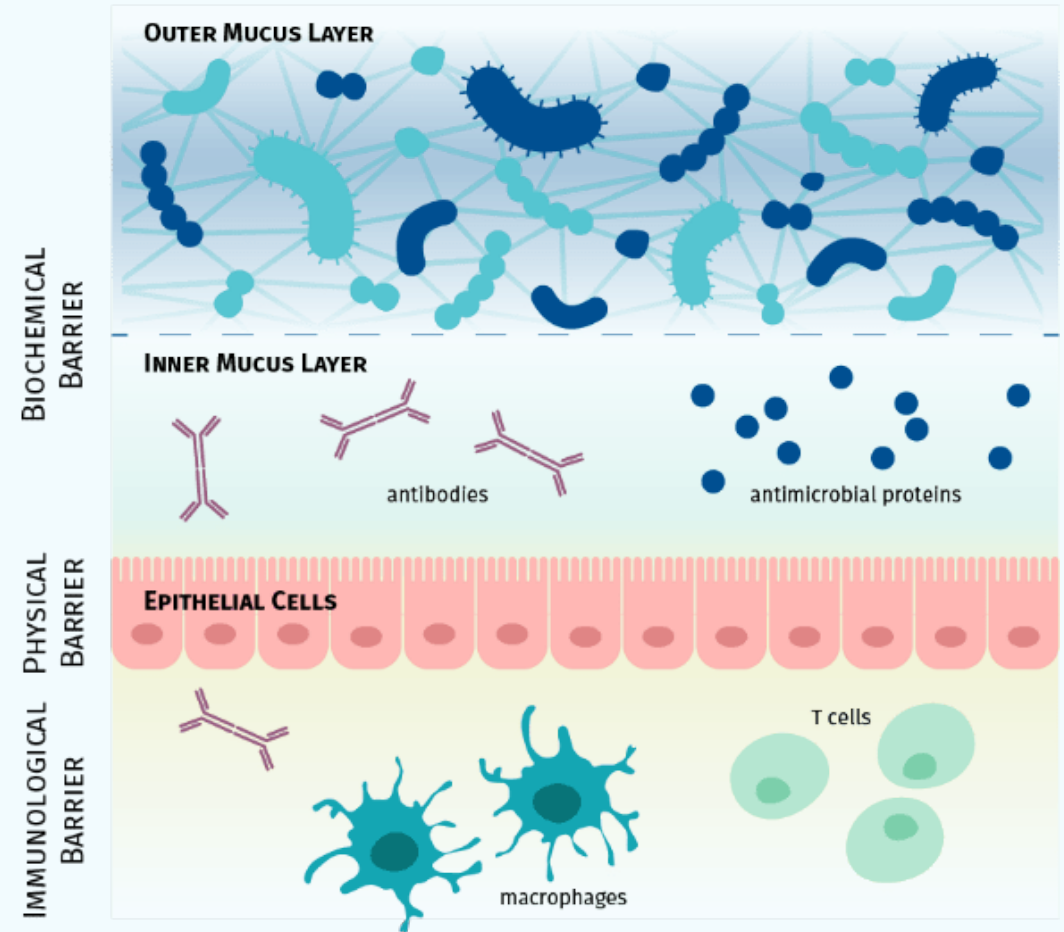


02

Bacterial **richness** and mucus layer prevent colonization by pathogens and improve gut barrier

# 80%

Cellular host defense localized in the gut



Cross-section of a healthy gut

# In Oncology, a Higher Gut Microbiome Diversity is Associated with Increased Survival<sup>1</sup>

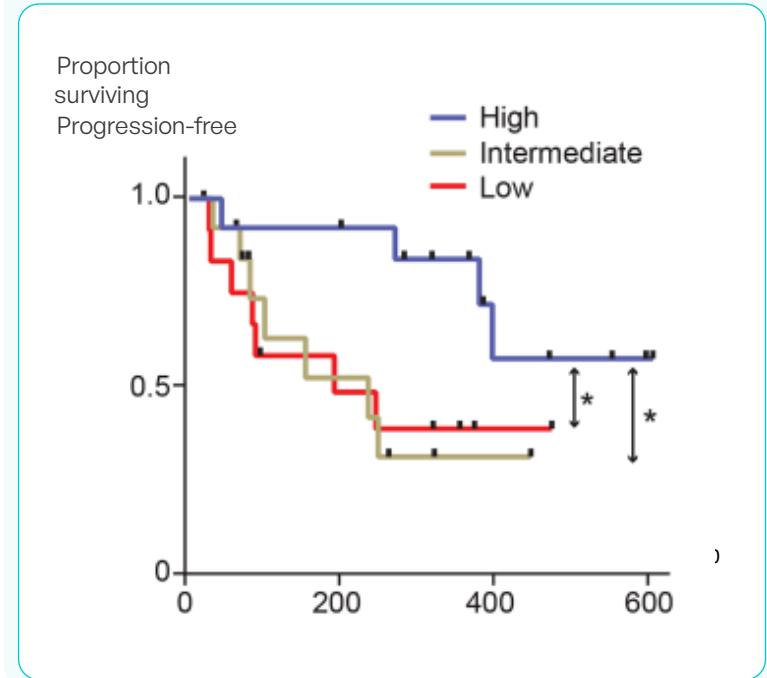
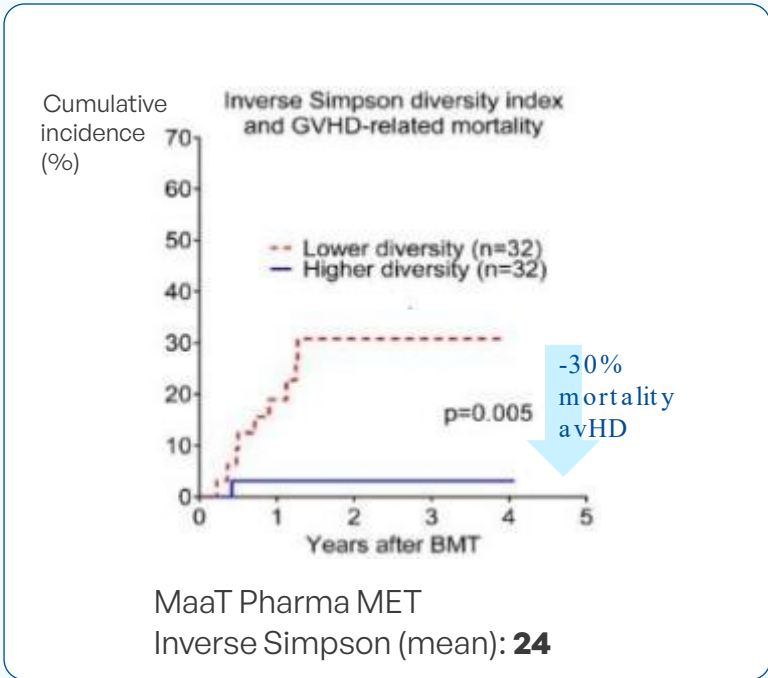
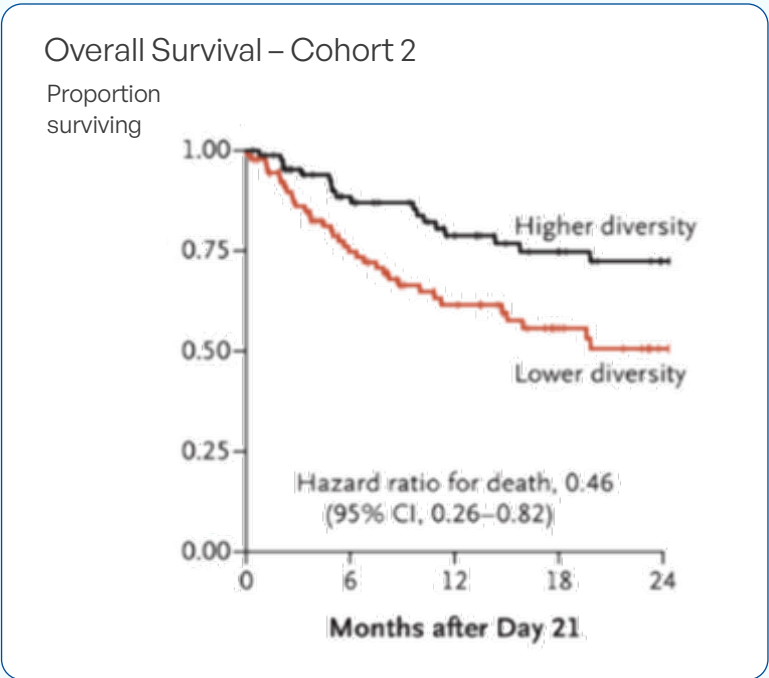
## Liquid Tumors

## Solid Tumors

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

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

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



<sup>\*</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;

# An Oncology Microbiome Platform Fueling a Deep Pipeline of Drug Candidates



Driving near-term value  
with the donor-derived MET-N platform

MaaT013

MaaT033



POOLING

MaaT013

MaaT033

Pooled microbiota

→ Maximized richness

→ Standardized (450 OTU ± 3%)

Progressing next-generation  
co-cultured scalable MET-C platform

MaaT034

MaaT03X

Original microbial ecosystem

▼

Master bank

▼

Working Bank

▼

Unlimited Co-Culture Scaling

MET-C product

↑

Multistep co-culture cGMP proprietary process

▼

Leading capabilities  
in microbiome drug production



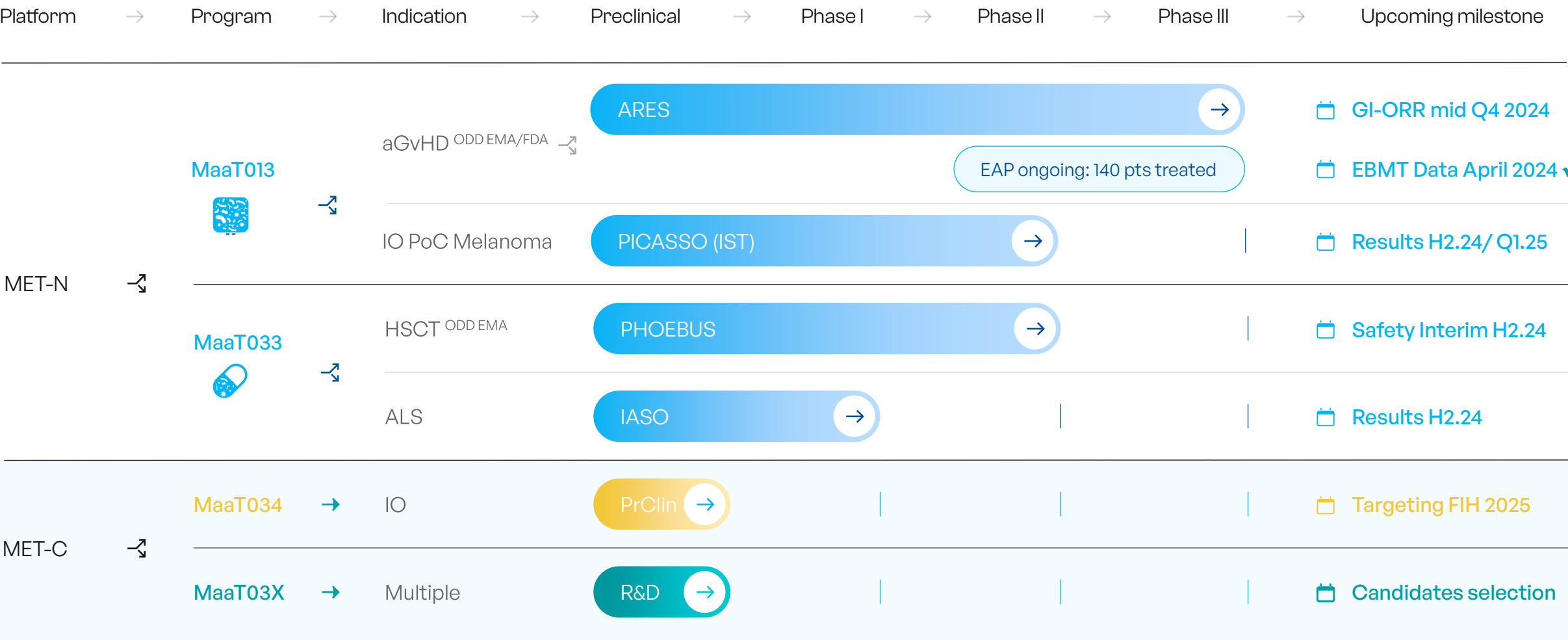
~10 000 treatable patients per year



MET-N / MET-C

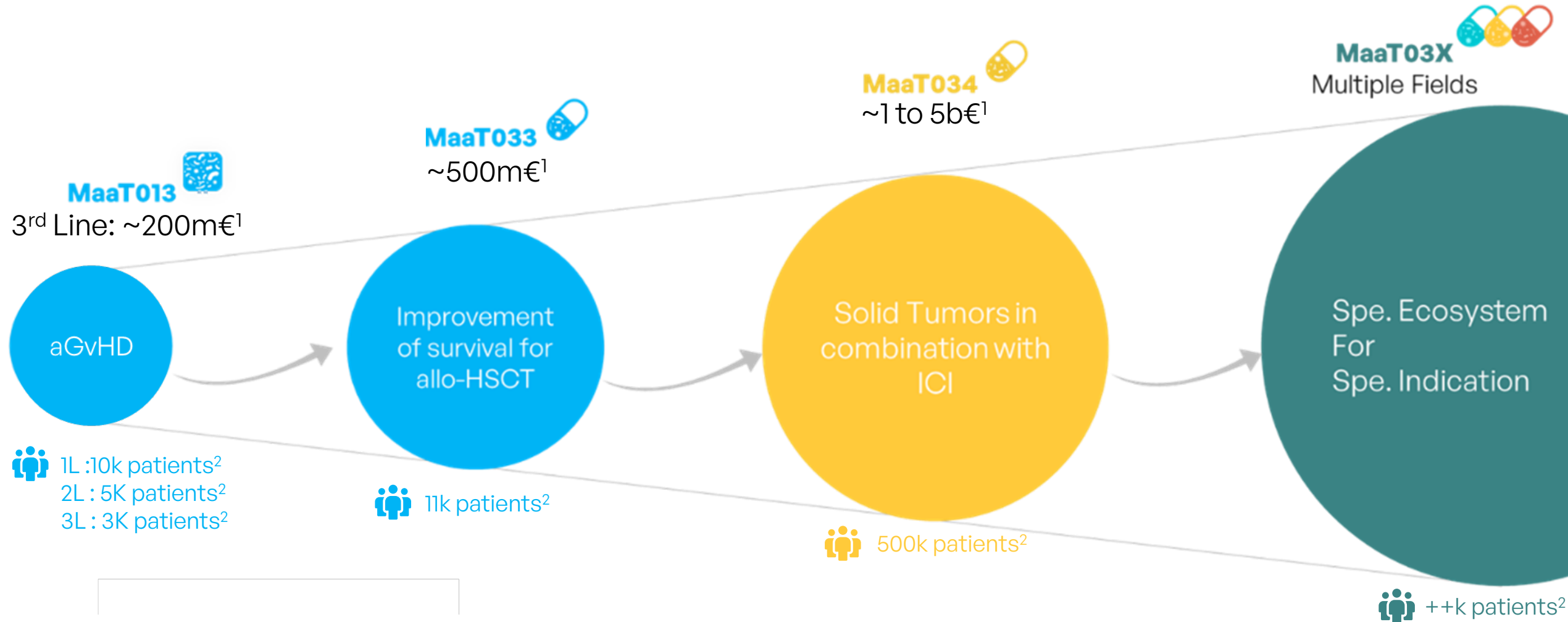


# A Strong Pipeline With Multiple Near-Term Value Inflection Milestones



aGvHD: acute Graft versus Host Disease ; IO: Immuno-Oncology ; PoC: Proof of Concept ; HSCT: Hematopoietic Stem Cell Transplantation ; ALS: Amyotrophic Lateral Sclerosis ; IST: Investigator Sponsored Trial

# Targeting Multiple Attractive Markets with Unmet Medical Need



<sup>1</sup>PYS EU5, US; <sup>2</sup>Per year

# Driving Near-Term Value with the Donor- Derived **MET-N** Platform

MET-N

# Microbiome Restoration with MaaT013: A Maximum-Density Product for Fast Engraftment in Acute Situations



- **Curative approach**
- MaaT013 has received **Orphan Drug Designation** from **FDA and EMA**
- **GI-ORR** in **mid Q4 2024**



01

Characteristics

**Pooled microbiota:** high-richness, high-diversity, full ecosystem  
Microbiome Therapy containing Butycore®  
**Non immunosuppressive treatment**



02

Current indication

**Gastrointestinal acute Graft-versus-Host Disease (GI-aGvHD)**  
~ 3k patients per year



03

Efficacy evaluation in EAP

**28-Days GI-ORR:** 52%  
**12-months OS:** 47%  
**18-months OS:** 42%  
**Data in all patients (n=140)**



04

Available Clinical Data

**HERACLES Phase 2** Clinical Trial, N=24, 2L  
**Early Access Program (EAP),** data from N=140, 3L-6L, program still ongoing  
**Ongoing ARES** – Positive **DSMB** review (n= 30)  
**> 250** patients treated to date

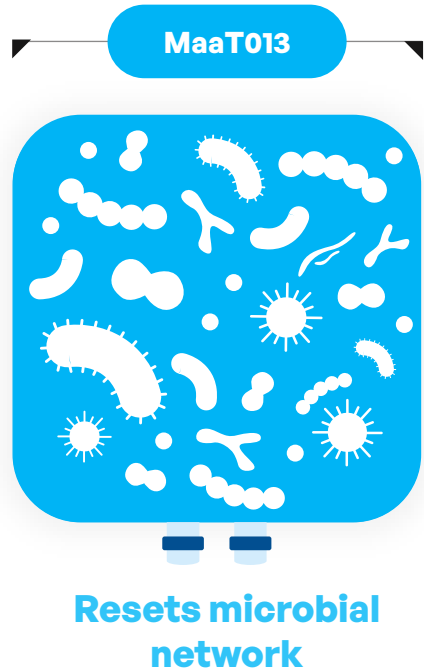


05

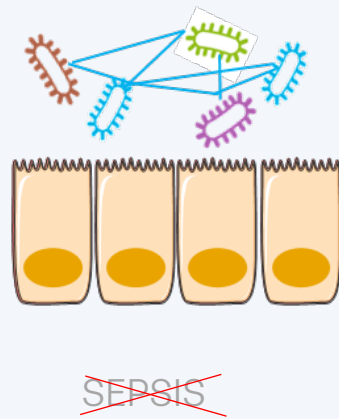
Administration

**3 doses** (enema bag) – within 10 days

# MaaT013, a Novel Agent to Treat aGvHD Acting by Restoring Immune Homeostasis and Gut Barrier Integrity



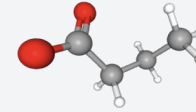
## 1 Restoration of barrier integrity



**Restoration of microbial homeostasis and network**

- Increasing diversity,
- Eradication of MDRB,
- Pathobiont growth inhibition

## 2 Production of immunoregulatory metabolites



- SCFA ( Butyrate, Propionate)
- Immunoregulation (IL-10...)

## 3 Modulation of immune homeostasis

### Regulatory T cells



- Immune homeostasis restoration
- Remission of symptoms

**Based on preclinical and ongoing clinical studies: MaaT013 could restore microbiome diversity, regenerates gut barrier's protective effect, and significantly curbs inflammation.**

# Unmet Medical Need: Acute Graft-versus-Host Disease (aGvHD) Resistant to<sup>1</sup> Steroids and Ruxolitinib (3<sup>rd</sup> line of treatment)

## Acute Graft-*versus*-Host Disease

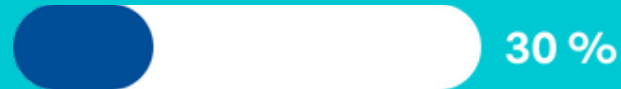
- > aGvHD is a condition where transplanted cells attack the recipient's body
- > Is life-threatening when not controlled by a treatment, and induces long-term complications for those who do survive



Affects 50% of stem cell transplanted patients, 10,000 people a year EU/US

## Treatment Paradigm

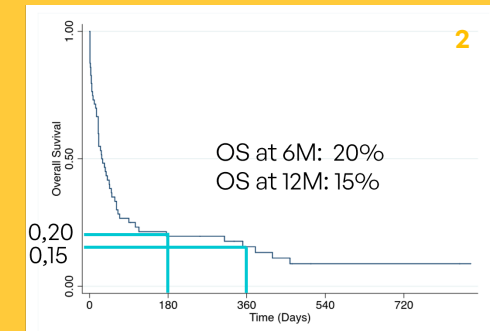
- > Corticosteroids are the 1<sup>st</sup> line of treatment, but 50% of patients do not achieve a sustained response
- > Ruxolitinib is approved as a 2<sup>nd</sup> line of treatment for SR-aGvHD (FDA, 2019 & EMA, 2022)



30% of aGvHD patients eligible for alternative treatment, primarily due to corticosteroids and ruxolitinib<sup>1</sup> resistance or non-eligibility  
Around 3,000 per year EU/US

## c. 30% of patients have no effective treatment option

- > There is **no** approved drug in 3L: lack of effective therapy
- > Off label options have shown limited benefit, showing the critical need for a new treatment



Outcome for this group of patients is dismal with a median survival of 28 days and a 15% OS at 1 year<sup>2</sup>

> Intestinal dysbiosis is associated with higher mortality in hemato-oncology<sup>3</sup>

# ARES, a Pivotal Phase 3 Trial to Treat aGvHD in 3<sup>rd</sup> Line Showing “*high efficacy and low toxicity*” as Concluded by the DSMB

ARES

## Patients with SR-GI-aGvHD

### Inclusion criteria

- Refractory or intolerant to 2L ruxolitinib
- Refractory to 1L corticosteroids
- aGvHD with GI symptoms
- Allo-HSCT
- Age > 18



Screening  
(D-14 to D-1)

Treatment Period D1, 5, 10

  
MaaT013 administration

D1

Primary efficacy evaluation  
GI-aGvHD ORR  
(CR+VGPR+PR)

EOT

D28

Primary follow-up

4th dose if relapse after response

M6

Long-term follow-up

M12

Overall  
Survival

D: Day, M: Month, EOT: End of treatment ; SR-GI-aGvHD: Steroid-refractory gastro-intestinal acute Graft-versus-Host Disease ; GI-ORR: Gastrointestinal Overall Response Rate; CR: Complete Response; VGPR: Very Good Partial Response; PR: Partial Response

\* DSMB review on 30 patients on October 2023



### DSMB\* main conclusions:

- Good safety profile
- ORR higher than pre-defined protocol



Commercial launch date  
anticipated in 2026



### Market potential:

~ 200 m€  
No Competitor in 3L

# The EAP Data Confirms Significant Improvement of Survival with High Level of Response



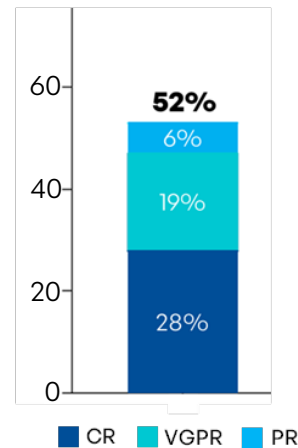
Data presented at EBMT 2024

## Global EAP populations

→ N=140, GI-aGVHD : 49% grade III, 40% grade IV, up to 6 lines of prior treatments (median 2) 121/140 received ruxolitinib

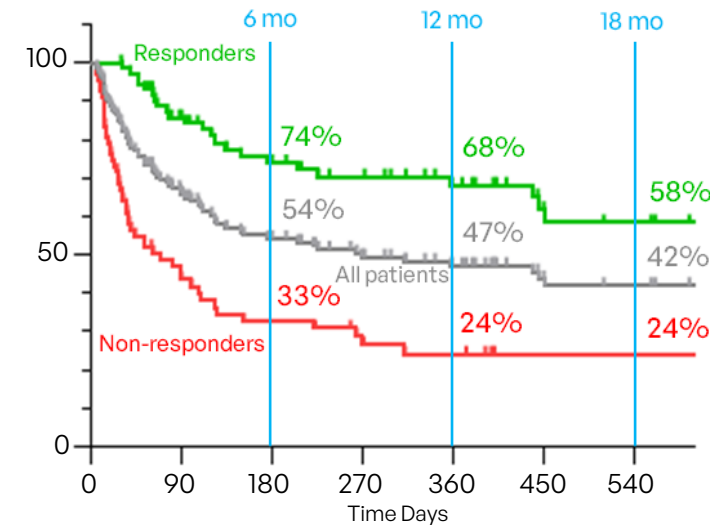
### GI-ORR

Patients (%)



### Overall Survival Rate

Survival (%)



- > High predominance of VGPR and CR responses in the EAP, suggesting a significant reduction in the disease burden
- > **Clinical response to MaaT013 translates to increased overall survival**

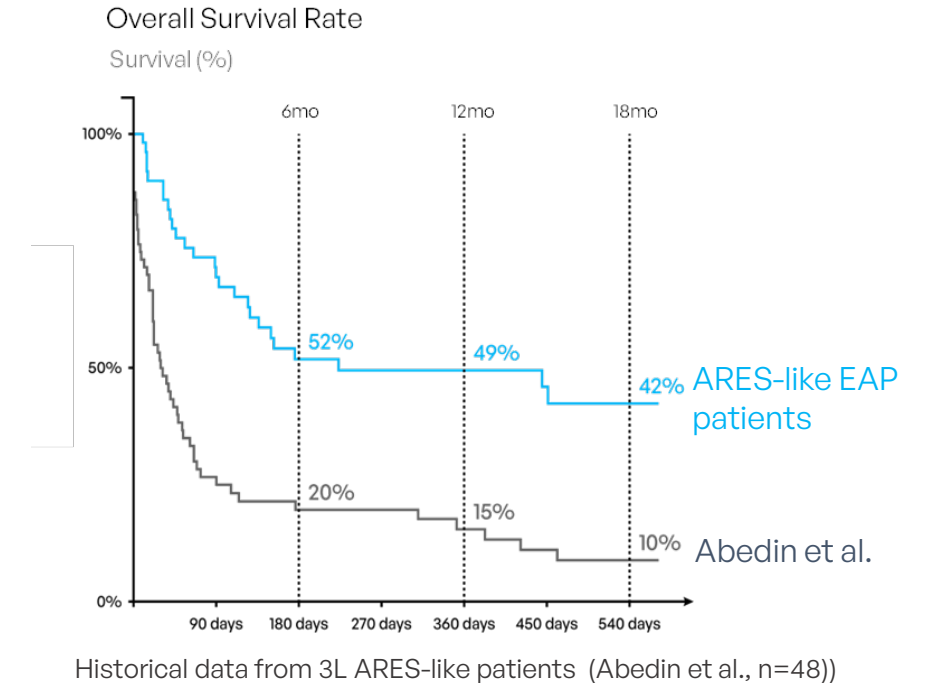
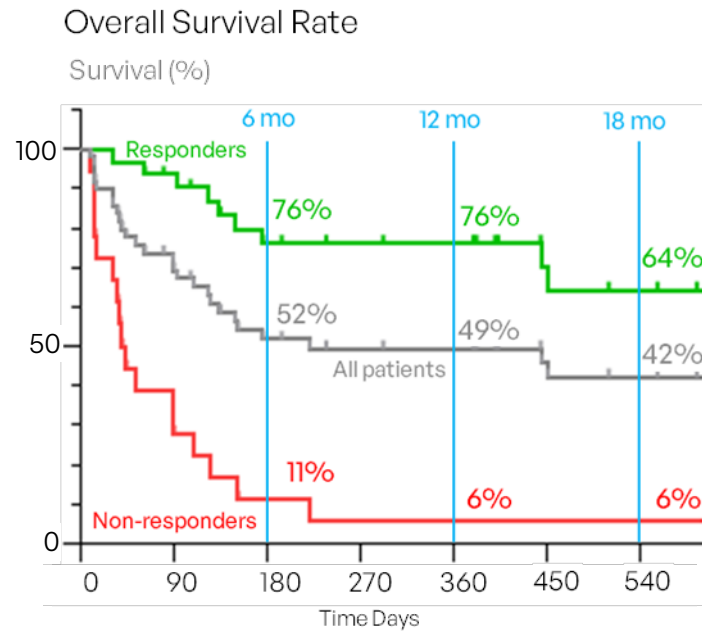
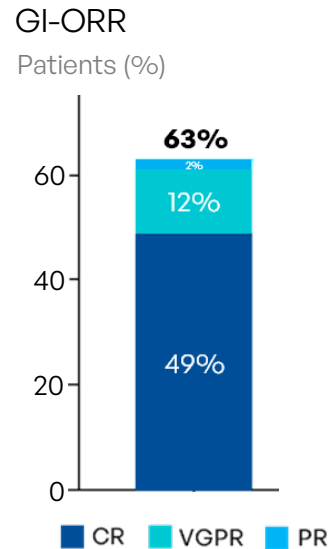
# The EAP Data Confirms Significant Improvement of Survival with High Level of Response

## EAP: ARES like populations

→ N=49, GI-aGVHD : 3L



Data presented at EBMT 2024



- No effective treatment in 3L with very low expected OS 2mo: 22% ; 6mo: 20% ; 12mo: 15%<sup>1</sup> confirming strong unmet medical need
- High predominance of VGPR and CR responses in the EAP, suggesting a significant reduction in the disease burden
- Good safety and high efficacy translating in a significant increase in overall survival compared to REACH1 and Abedin et al. data - 2021<sup>1</sup>

<sup>1</sup>Expected OS of Steroid and Ruxolitinib resistant aGvHD patient at : 2 mo: 22% (REACH1 trial), 6mo: 20% and 12mo: 15% (Abedin et al.)  
Abbreviations: CR, complete response; VGPR, very good partial response; PR, partial response



## Proof-of-Concept with MaaT013 in Combination with ICI In Metastatic Melanoma

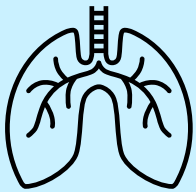


Serves as PoC for MaaT034 in  
combination with ICI

MET-N

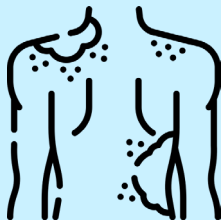
## Checkpoint Inhibitors have revolutionized treatment of Solid Tumors but a large proportion of patients can't benefit from it due to primary resistance

### Primary Resistance Rate to Immune Checkpoint Inhibitors



Lung Cancer (NSCLC)

**35 - 40 %**



Skin Cancer (Melanoma)

**Up to 65 %**



Around 19 million people diagnosed with cancer each year globally



Immune Checkpoint Inhibitors (ICI) significantly improved outcomes of patients with solid tumors and strategies to enhance responses remains **a strong unmet medical need.**



**Combination strategies** tested so far to improve responses to ICI remains mostly unsuccessful and/or associated with a **higher toxicity.**

→ **Urgent need to bring new combination therapies with ICI to safely increase the response rates and overall survival**

## Growing clinical evidence that a Full-Ecosystem Gut Microbiome influences efficacy of ICI

**2021**

**FMT from ICI-responders could overcome resistance to ICI in non-responders with metastatic melanoma**

✓ **6/15**

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

✓ **3/10**

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

**2023**

**FMT from healthy donors increases response of aPD1 in ICI-naïve patients with metastatic melanoma**

✓ **13/20**

**ICI-naïve** → Responders  
(ORR=65 %, Routy et al. 2023)

**2024**

**Microbiotherapy from healthy donors increases response of aPD1+aCTLA4 in ICI-naïve patients with metastatic melanoma**

✓ **15/20**

**ICI-naïve** → Responders  
(ORR=75 %, Routy, . 2024)

○ **.../35**

**First RCT**  
**70 pts rand 1:1**  
(MaaT Pharma)

*aPD1 historical response close to 33 %*

*aPD1+aCTLA4 historical response close to 59 %*

FMT = (Hospital) Fecal Microbiota Transplantation

→ Leveraging the complete gut microbiome properties may be a game-changer in immuno-oncology

# MaaT013 Evaluated in Phase 2 Randomized Clinical Trial in Melanoma

## Recruitment completed Ph. 2a PICASSO trial

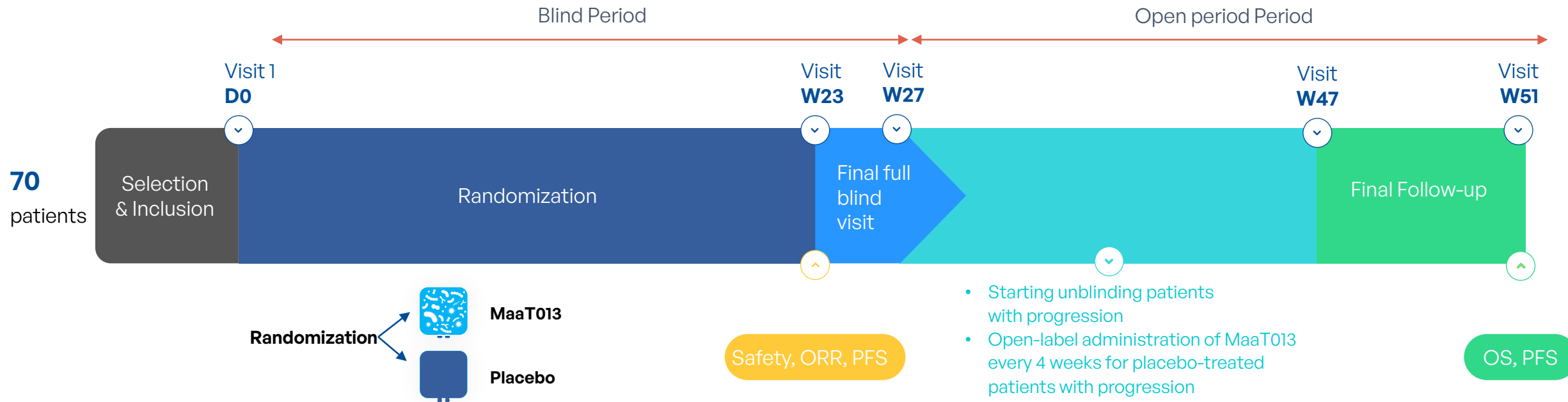
**Investigator led trial** (Assistance Publique - Hôpitaux de Paris – sponsor) and in collaboration with Institut Gustave Roussy

- RCT [MaaT013 + ICI] vs. [Placebo + ICI] in 70 metastatic melanoma patients
- **Data expected H2.24/Q1.25**

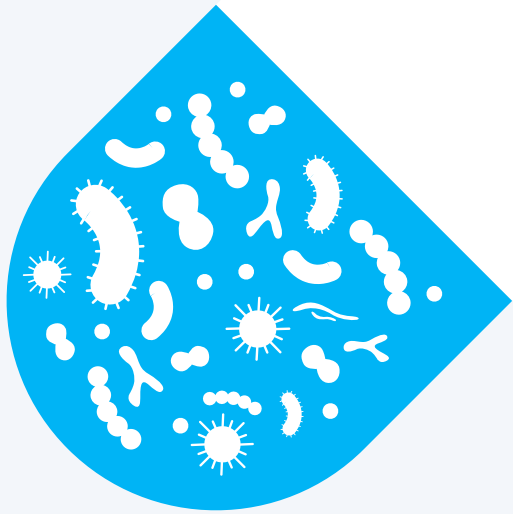
## Key study endpoints after 23 weeks of treatment:

- 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

### PICASSO RCT design



# Ensuring Optimal Microbiota Function: MaaT033 – The Oral Ecosystem Microbiome Capsule for Adjunctive and Maintenance Therapy



- **Adjunctive and Maintenance**
- **Targeted release oral Capsules**
- MaaT033 has **received Orphan Drug** from the **EMA**



01

## Characteristics

**Pooled microbiota** : high-richness, high-diversity, full ecosystem,  
**Microbiome Ecosystem Therapy containing Butycore®**  
**Non immunosuppressive** treatment



02

## Current indication

**Improving survival of allo-HSCT patients** (blood cancers i.e leukemia, ...) – ~ 11k patients per year  
**Slowing down disease progression in ALS**



03

## Clinical Program

**Ongoing Phase 2b trial PHOEBUS** in allo-HSCT patients  
**Phase 1b trial IASO** ongoing in ALS



04

## Administration

**Oral** (a lyophilized capsule)

# MaaT033: a Potential Adjunctive Treatment for Patients Receiving allo-HSCT



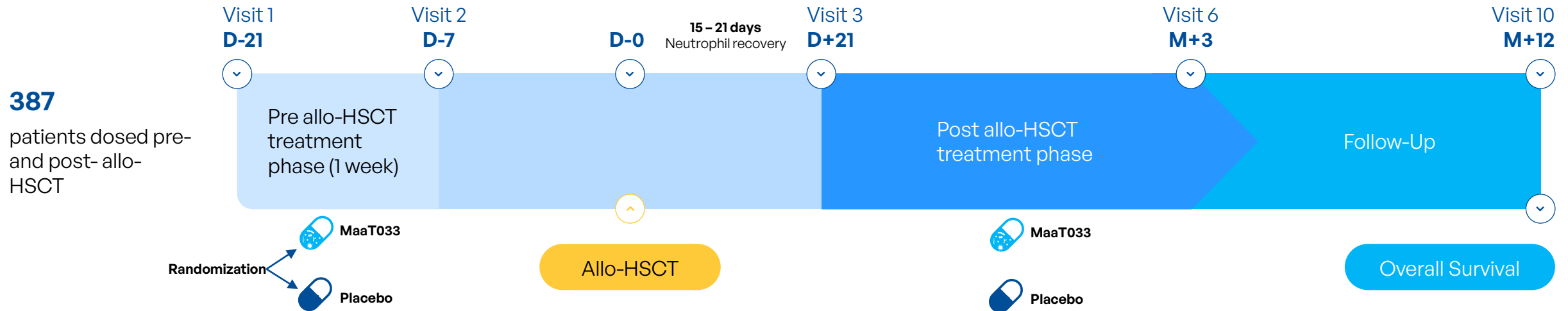
→ **387** patients in a **randomized, double-blind, placebo-controlled international** study

→ **56 sites** targeted globally

→ First positive DSMB (n=20\*) in July 2024 – safety DSMB are planned every 6 months throughout the study

→ Primary endpoint: **efficacy** of MaaT033 in **improving overall survival at 12 months**

→ Study started in **November 2023**, results are expected in **2026**



<sup>1</sup> Expansion to US sites subject to discussion with the FDA

\*cutoff date: April 2024



Ongoing Phase 2b  
PHOEBUS



Safety Interim analysis on  
60 patients in H2 2024



Based on expected duration  
of recruitment, OS primary  
endpoint expected in 2026



~ 11k patients  
per year

# MaaT033 Aims to Slow Down Amyotrophic Lateral Sclerosis Progression



## Amyotrophic Lateral Sclerosis

- Could affect up to 60,000 patients in US & EU by 2040<sup>1</sup>
- Paralysis and death 3 to 5 years after diagnostic<sup>2</sup>
- Currently no curative treatment and few symptomatic treatments

## Rationale for Exploratory Utilization of MaaT033 in ALS

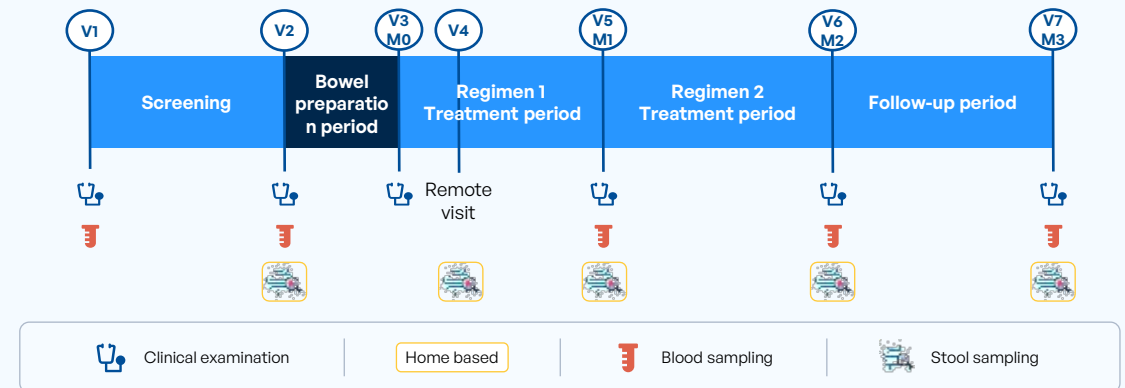
- Microbiota-Gut-Brain axis has the potential to become the new standard to treat neurodegenerative diseases, including ALS
- MaaT033 safety profile and oral administration is suitable for ALS
- Strong support from medical community & patients
- A cost-effective way of testing neurodegenerative field in an indication with high medical need

<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/>

## Study

- Up to **15 patients** in a **pilot, open-label, Phase 1b** study **in France**
- **Key study endpoints:** assess safety and tolerability of MaaT033 and gut microbiota composition evolution
- Study started in **2023** → **Results** expected in **H2 2024**
- **Positive DSMB in Feb. 2024:**  
Trial to proceed as planned without modifications  
Good safety profile and generally well tolerated



Study  
developed with:



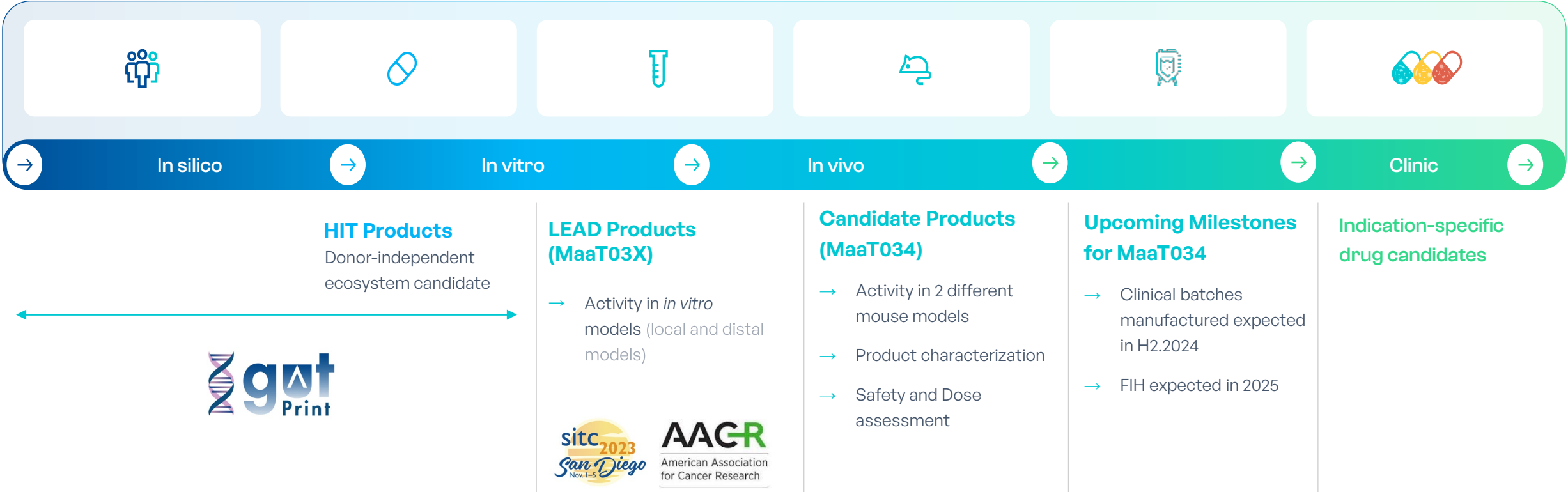
In collaboration  
with:



# Progressing the Next- Generation, Co-Cultured, Donor Independent **MET-C** Platform

MET-C

# MET-C Product Generation is Driven by MaaT Pharma’s Proprietary Predictive AI, Eubiotic Score and *in vitro* and *in vivo* validation processes



# End-to-End In-house cGMP Manufacturing

All MET

# Europe's Largest Specialized cGMP Manufacturing Facility for Microbiome Ecosystem Therapies

A dedicated 1,600m2 site (expandable) to support demands until 2034 for MET-N clinical and future commercial production, R&D, and clinical batches of MET-C products (MaaT034 & MaaT3X family) (est. first step):

~10 000 treatable patients per year

MaaT013

9,000  
pouches / year

MaaT033

1,300,000  
capsules / year

MaaT03X

Up to 300,000  
capsules / year

01

Fully integrated Manufacturing and development platform for a streamlined product development, scaleup and GMP process.

02

Ongoing CSR global strategy: reforestation program in France (GoGreen) and “Cap Vert pour la forêt” program, etc.

03

Option to expand manufacturing facilities to double manufacturing capabilities.

Status

Production started in September 2023



Partnership  
with



# Key Takeaways

# Multiple Near-Term Value Inflection Milestones

2024

## MaaT013 (pooled enema)

GvHD | EAP long term follow-up EBMT24 ✓  
GvHD | ARES P3 GI-ORR mid Q4 24  
IO Mela. | PICASSO P2a Results H2.24/Q1.25

## MaaT033 (pooled capsule)

HSCT | PHOEBUS P2b Safety Interim DSMB H2  
& 6-month DSMB Study follow-up  
ALS | IASO P1b Results H2

## MaaT034 (co-cultured capsule)

Candidate Selection  
1<sup>st</sup> Clinical Batch Manufactured

2025

## MaaT013 (pooled enema)

GvHD | Final Results (OS)

## MaaT033 (pooled capsule)

HSCT | PHOEBUS P2b Safety 6-month DSMB  
Study follow-up

## MaaT034 (co-cultured capsule)

Solid Tumors IO | Target FIH 25

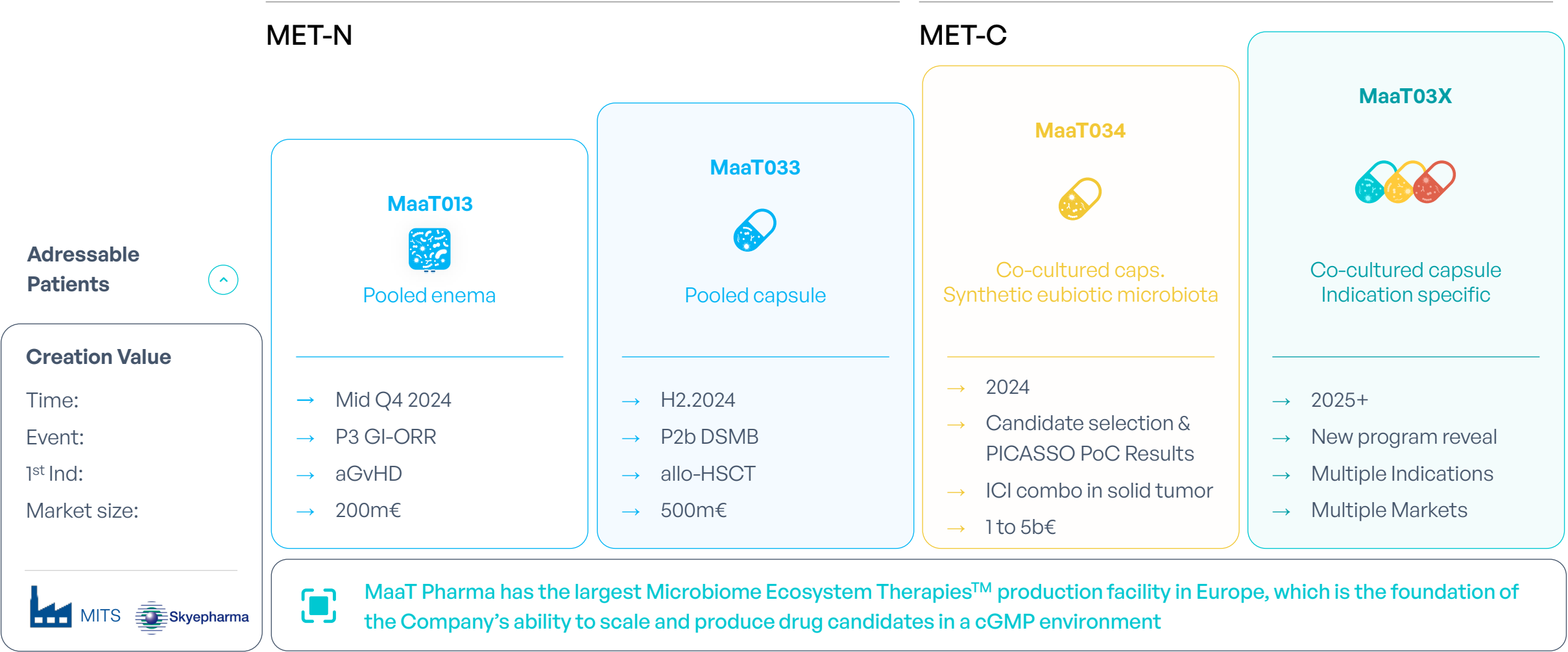
## MaaT03X (co-cult. ind.-spec. caps)

Undisclosed | Next Steps

Finance

- **Revenues of MaaT013 in aGvHD of 2.2m€** for 2023 from Early Access Program
- **Cash position of 18.2m€** as of March 31, 2024. **Post follow-on in May 2024, (approx. €17.3m€) cash runway** extends into **early Q1/2025**
- **Exploring options to extend cash runway**, including non-dilutive and dilutive sources

# A Robust Value Creation Strategy Driven by Leading Expertise in Microbiome-based Therapeutics



# 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.**

## 2023 CSR indicators

Social

34 y-o

is the average age of permanent employees

36%

Percentage of PhD, PharmD, MD among employees involved in research

75%

Training Plan Completion Rate

Environment

2394 tCO2e

Carbon footprint

361 kWh /Employee

Energy consumption per employees on site

Societal

85%

of operating expenses related to R&D as a proportion of total operating expenses

259

public interventions to increase awareness on microbiome

Governance

38%

of women in the Board of directors

72%

of women in the Executive team

The background of the slide is filled with various stylized, colorful illustrations of microscopic organisms, including bacteria, viruses, and fungi, in shades of blue and teal. The Ma Pât logo is located in the top center.

Ma  
Pât

# Thank you

[invest@maat-pharma.com](mailto:invest@maat-pharma.com)

CORPORATE  
PRESENTATION