



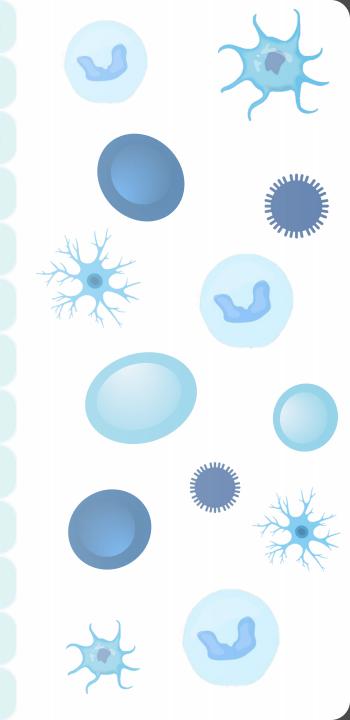
# Enhancing Survival Through Innovative Immune Modulation

December 2024









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### Success in Refractory GvHD Will Pave the Way for Broad Therapeutic Advances



# Breakthrough advances of MaaT013 in GvHD

- Recruitment completed for **Phase 3**in aGvHD in Europe, expecting primary
  endpoint readout in January 2025
- Unprecedented data from Early Access Program (n=154) will be presented in December at ASH 2024 (1y OS 47% vs 15% historical data, 42% at 2y)
- First-in-Class treatment modality in the U.S. supported by an open IND enabling enhanced patient access



#### Deep oncology pipeline

- Full ecosystem donor-derived and coculture platforms driving candidate development with 2 clinical and 1 preclinical assets
- gutPrint® AI, linked to co-culture platform, poised to deliver, potentially, clinically-ready candidates by 2026
- Largest European cGMP production facilities for Microbiome Ecosystem
  Therapies







- Finance
- Leadership in refractory GvHD EAP with revenues of MaaT013 of 2.3m€ for the nine first months of 2024 compared to 1.8m€ in 2023
- Cash position of 27m€ as of September 30, 2024. Post follow-on in May 2024, (approx. €17.3m€) cash runway extends into Q2/2025
- Exploring options to extend cash runway, including non-dilutive and dilutive sources

# Management Team



Hervé Affagard

Co-Founder & CEO





**Eric Soyer** 

Chief Financial
Officer





Gianfranco Pittari, MD, PhD

Chief Medical Officer







Carole Schwintner, PhD

Chief Technology Officer





**Sian Crouzet** 

Chief of Staff





Jonathan Chriqui, PharmD

Chief Business
Officer





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### Oncology-Focused Platform Fueling a Deep Pipeline of Drug Candidates





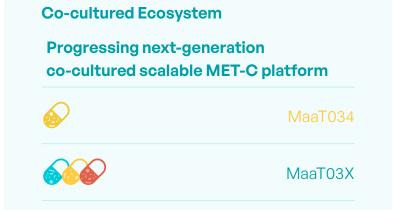
Driving near-term value with the donor-derived MET-N platform



MaaT013



MaaT033





#### **In-house Production**

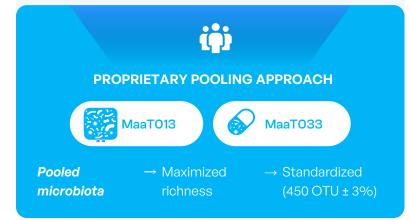
Leading capabilities in full ecosystem microbiome drug production



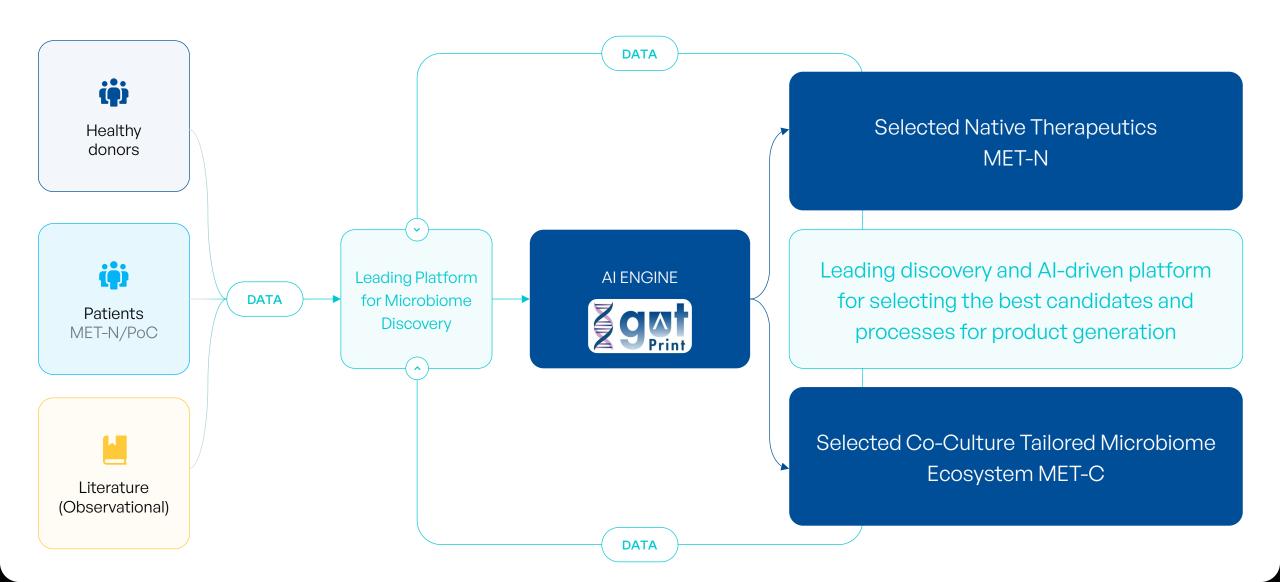


Capacity: ~11,000 treatable patients per year





# Al-driven Research Engine Powered by Metagenomics Enabling Candidate Selection



# Improving Disease Outcomes Through Microbiome Repair: GvHD and Beyond

# Multiple Drivers of Microbiome Disruption

- Antibiotics
- Chemotherapy
- Radiation therapy
- Medications
- Infections
- Chronic Disease
- Poor Diet
- Toxins
- Others

# **Local and Systemic Effects of Dysbiosis**

- Loss of Microbial Diversity
   Associated with pathogenic invasion and inflammation
- Gut Barrier Dysfunction

  Harmful microbes can overgrow and pass
  through the gut lining into the bloodstream
- > Immune Homeostasis Disruption Causing an overactive or underactive immune response

# Restoring Health Through Microbiotherapy

- Rebuilding Gut Microbial Diversity

  Improves resilience to pathogens and
  enhances metabolic functions
- Repairing Gut Barrier Integrity

  Prevents pathogens from entering the bloodstream
- Rebalancing Immune Function
  Leads to decreased inflammation and
  restoration of immune homeostasis

#### Innovative approach with multiple areas of clinical application

Current:

→ |

Hemato-Oncology (GvHD, HSCT)

(>)

Immuno-Oncology (overcoming resistance to immuno-oncology therapeutics)

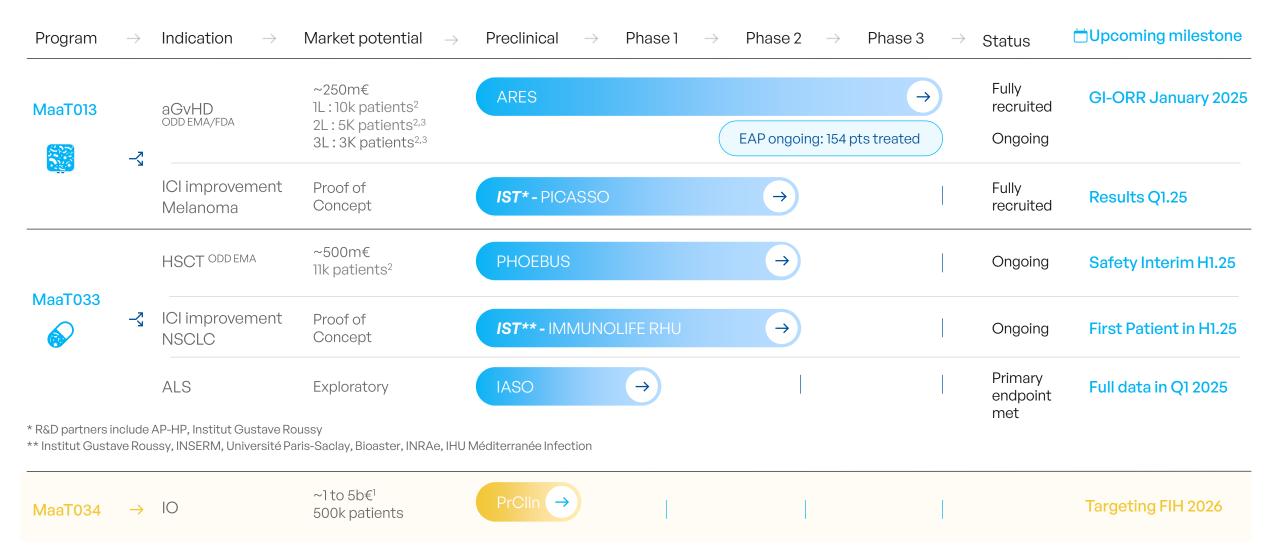
Tomorrow:

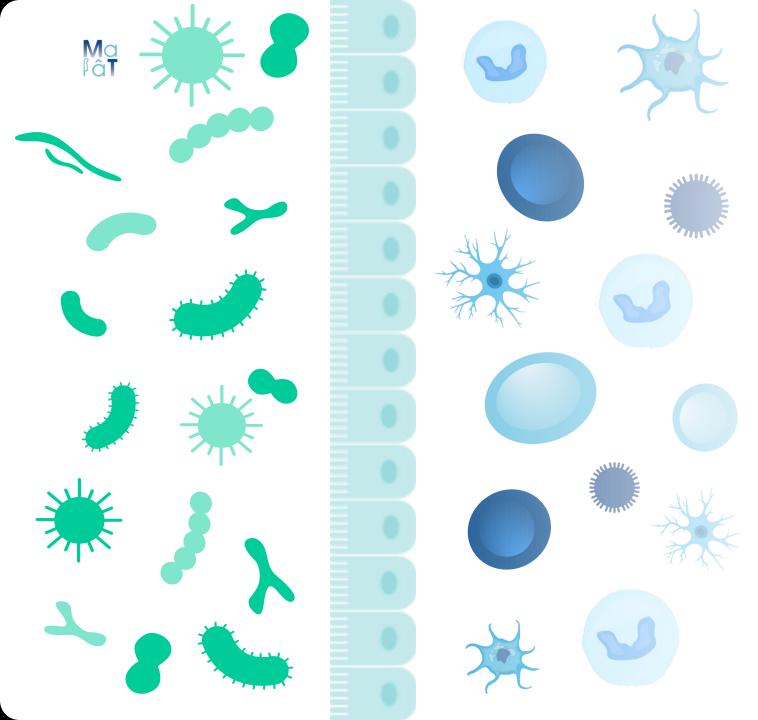
Autoimmunity

Gastroenterology

Neurodegenerative Diseases... and more

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





# Program Overview



# Understanding and Addressing Acute Graft-versus-Host Disease (aGvHD)

- → A significant complication following allogeneic hematopoietic stem cell transplantation (AlloHSCT)
- → It may occur in 50% of patients undergoing AlloHSCT, typically presenting within the first 100 days post-transplant

In aGvHD, donor immune cells recognize the recipient's tissues as foreign leading to an immune-mediated attack

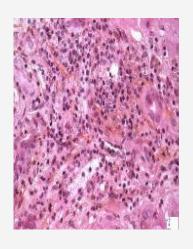
Common clinical manifestations typically involve the gastrointestinal tract, the skin and the liver

#### **GIGVHD**



Severe diarrhea, abdominal pain

#### **Liver GvHD**



Jaundice, liver dysfunction/failure

#### **Skin GvHD**



Skin: Rash, itching



GvHD Patients / year



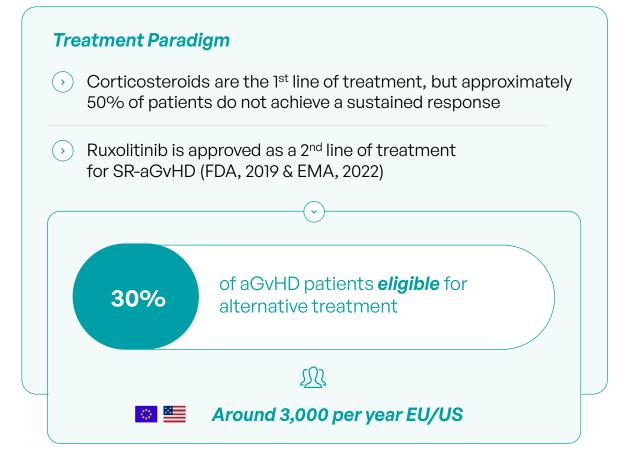




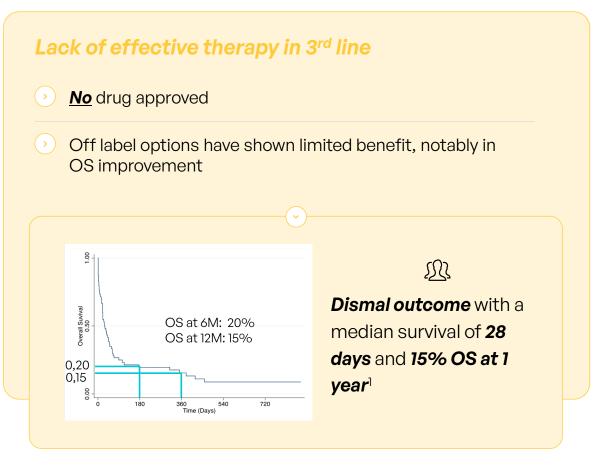
1 year mortality in 3L+1







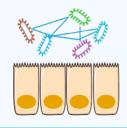
→ Quick action



- → GvHD is characterized by intestinal dysbiosis which is associated with higher mortality in hemato-oncology<sup>2</sup>
- → Microbiota shows potential for use in other treatment lines, as demonstrated by EAP patients treated from second to sixth

### Microbiome Modulation to Restore Immune Homeostasis and Gut Barrier Integrity

#### Restoration of barrier integrity<sup>1</sup>

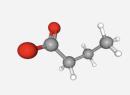


# Restoration of microbial homeostasis and diversity

Eradication of MDRB

Pathobiont growth inhibition

#### **Production of immunity-regulating metabolites<sup>2</sup>**



Short-Chain Fatty Acids (e.g., Butyrate, Propionate)

#### Modulation of the functional homeostasis in T cell subsets<sup>3</sup>



Treg sequestration to the gut

Th17 and Treg balance

- → Anti-inflammatory cytokines (IL-10...)
- $\rightarrow$  Pro-inflammatory cytokines (IL-6, TNF- $\alpha$ )



#### aGvHD Resolution4

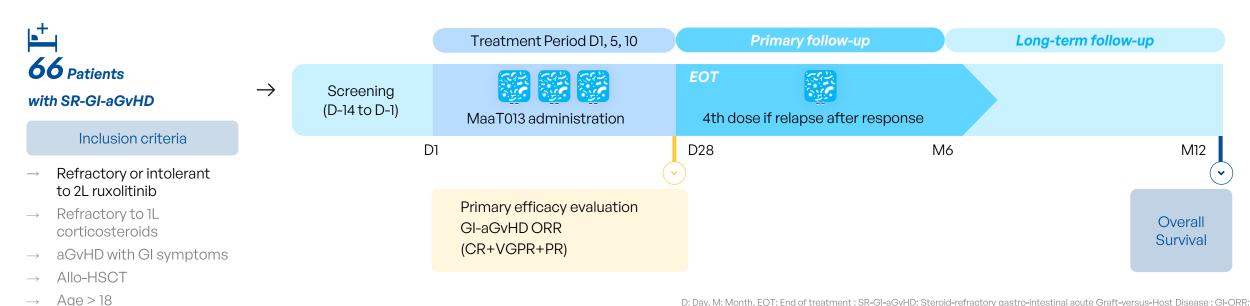




# ARES, a Pivotal Phase 3 Trial to Treat aGvHD in 3<sup>rd</sup> Line Showing *"high efficacy and low toxicity"* as Concluded by the DSMB with Topline in January 2025



Upcoming milestones: GI-ORR expected in January 2025 | OS expected by end of 2025 | Regulatory submission expected in 2025



D: Day, M: Month, EOT: End of treatment; SR-Gl-aGvHD: Steroid-refractory gastro-intestinal acute Graft-versus-Host Disease; Gl-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



Marketing authorisation anticipated in 2026



Market potential: ~ 250 m€

No Competitor in 3L

14

ARES-like

**EAP** patients



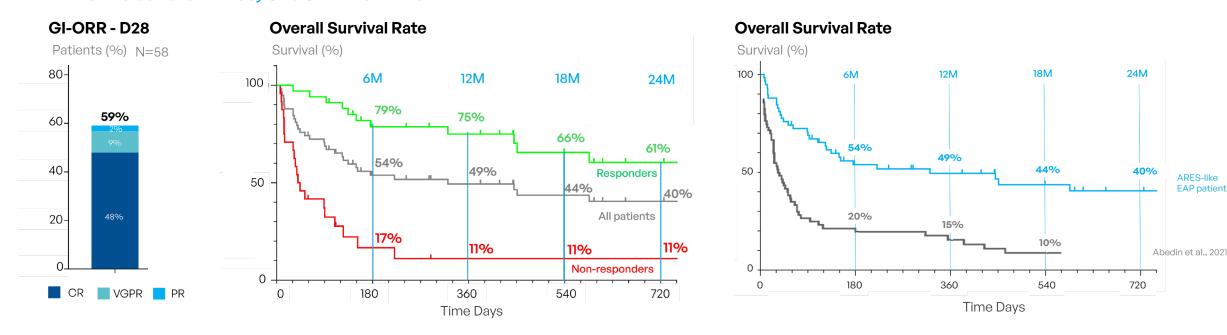


# In 3<sup>rd</sup> Line, the EAP Data Confirms Frequent Responses to MaaT013 Leading to Prolonged Survival



#### MaaT013 in aGvHD is well tolerated with a favorable benefit / risk profile to date

EAP: ARES like cohort - N=58, GI-aGvHD: 3rd Line



Historical data from 3L ARES-like patients (Abedin et al., 2021 n=48)

- No effective treatment in 3<sup>rd</sup> line with **very low expected OS** 6mo: 20%; 12mo: 15%<sup>1</sup> confirming strong unmet medical need
- Observed responses (VGPR &CR) are almost invariably at D28, indicating prompt and significant aGvHD control
- Remarkable improvement in overall survival (18-mo OS 44% vs 10% historical data) compared to REACH1 and Abedin et al. data 2021





# Unlocking the Potential of Checkpoint Inhibitors: How Full-Ecosystem Gut Microbiome Overcomes Primary Resistance

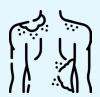
Immune Checkpoint Inhibitors (ICI) significantly improve outcomes in solid tumor patients

**Primary Resistance Rate to ICIs** 



Lung Cancer (NSCLC)

35 - 40 %



Skin Cancer (Melanoma)

**Up to 65 %** 

→ Urgent need for new ICI combination therapies to boost response rates and survival

Leveraging full ecosystem microbiome could be a game-changer in immuno-oncology

2021: FMT from ICI-responders could overcome resistance to ICI in non-responders with metastatic melanoma



**⊘** 6/15

**⊘** 3/10

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

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



2023: Microbiotherapy from healthy donors boosts response to aPD1+aCTLA4 in ICI-naive metastatic melanoma patients



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



PICASSO studying MaaT013: 1st multicenter **RCT 70 pts rand 1:1** 

### MaaT013 Evaluated in Phase 2 Randomized, Multicenter Clinical Trial in Melanoma

#### Phase 2a PICASSO trial, fully recruited

*Investigator Sponsored Trial* (Assistance Publique - Hôpitaux de Paris) in collaboration with Institut Gustave Roussy

→ Data expected Q1.25

#### Key study endpoints after 23 weeks of treatment:

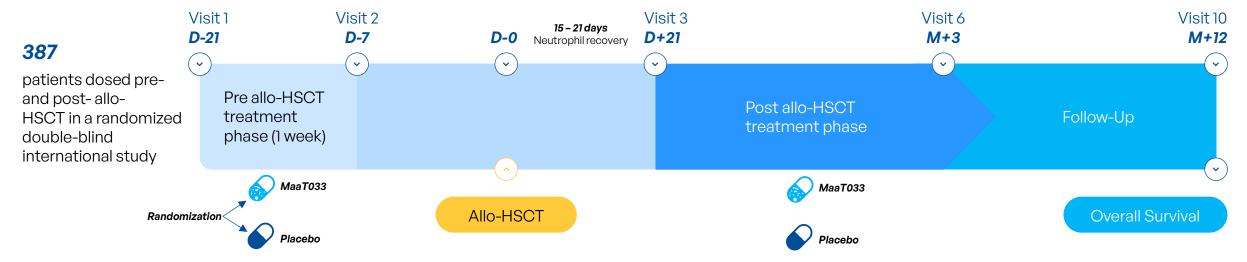
MaaT013 safety profile and best-overall response rate vs placebo as add-on treatment to Ipilimumab + Nivolumab



# MaaTO33: Phase 2b PHOEBUS Trial Exploring a Potential Adjunctive Treatment for allo-HSCT Patients

Design presented at EBMT and ASH

- First positive DSMB (n=20\*) in July 2024 safety DSMB are planned every 6 months throughout the study - Next anticipated January 2025
- Primary endpoint: efficacy of MaaT033 in improving overall survival at 12 months
- Study started in **November 2023**



Expansion to US sites subject to discussion with the FDA

\*cutoff date: April 2024



**Ongoing Phase 2b PHOEBUS** 



Safety Interim analysis on 60 patients expected in H12025



Based on expected duration of recruitment, OS primary endpoint expected in 2027



~ 11k patients per year

### MaaT033: Targeting Amyotrophic Lateral Sclerosis Progression





#### Amyotrophic Lateral Sclerosis (ALS)

- $\rightarrow$  Could affect up to 60,000 patients in US & EU by 2040  $^{1}$
- → 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 MaaTO33 in ALS

- Microbiota-Gut-Brain axis is a multifactorial MoA which has the potential to become the new standard to treat neurodegenerative diseases, including ALS
- → Strong support from medical community & patients
- A capital efficient way of testing neurodegenerative field in the most severe indication with high medical need with potential for expansion

- Study
- → Up to 15 patients in a pilot, open-label, Phase 1b study in France
- → **Key study endpoints**: safety and tolerability of MaaT033 | gut microbiota composition evolution | marker showing potential impact on disease progression
- → Study fully recruited in H1 2024

→ Full data readout in *H1 2025* 

- → Positive DSMB in Feb. 2024
- → Primary endpoint met in Nov. 2024
- Good safety profile and generally well tolerated
- Successful engraftment of MaaT033
- DSMB supports proceeding to Phase 2

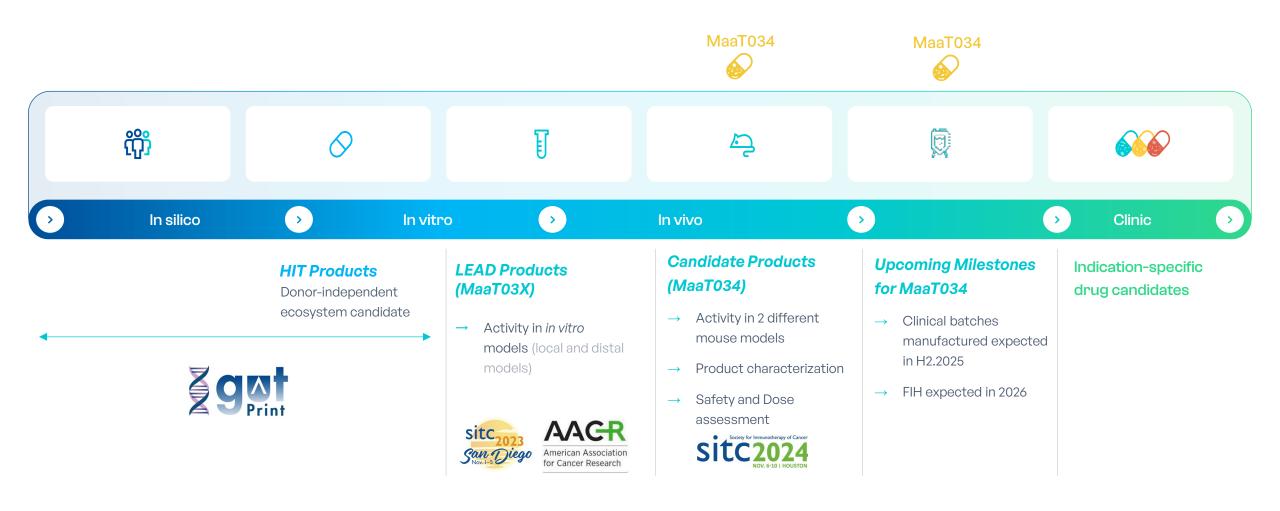


<sup>&</sup>lt;sup>1</sup> Arthur, K., Calvo, A., Price, T. et al. Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. Nat Commun 7, 12408 (2016). https://doi.org/10.1038/ncomms12408

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



# MET-C Product Generation is Driven by MaaT Pharma's Proprietary Predictive Al, Eubiotic Score and *in vitro* and *in vivo* Validation Processes



# All MET



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

A dedicated 1,600m<sup>2</sup> site (+17,000 sq ft), 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)

~11,000 treatable patients per year

MaaT013

9,000

bags/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

Option to expand manufacturing facilities to double manufacturing capabilities.



**Status** 

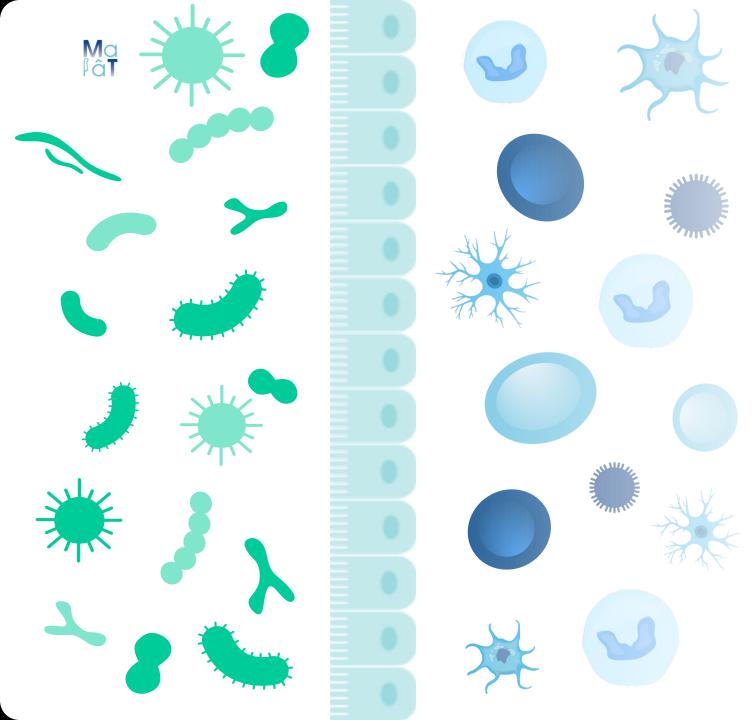
Production started in September 2023 Currently used at 10% capacity Scalable up to commercial capacity



**Partnership** with







# Key Takeaways

### Multiple Near-Term Value Inflection Milestones

Q4 2024 / 2025

#### MaaTO13 (pooled bag)

- GvHD | EAP Update **ASH24** ✓
- GvHD | ARES P3 GI-ORR January 25
- IO Mela. | PICASSO P2a Results **Q1.25**
- GvHD | ARES Final Results (OS) **H2 25**
- GvHD | Filing to EMA

#### MaaTO33 (pooled capsule)

- ALS | IASO P1b Primary Endpoint Q4 24 ✓
- ALS | IASO P1b Full data readout Q1 25
- HSCT | PHOEBUS P2b Safety 6-mo DSMB Q125
- HSCT | PHOEBUS P2b 60/120 pts DSMB H1/H2 25
- NSCLC | IMMUNOLIFE P2a FPI H1 25

#### MaaTO34 (co-cultured capsule)

- · Selection of candidate
- 1st Clinical Batch Manufactured H2 25

2026+

#### MaaT013 (pooled bag)

• GvHD | EMA Marketing Authorization

#### MaaT033 (pooled capsule)

- HSCT | PHOEBUS P2b Satefy 6-mo DSMB
- HSCT | PHOEBUS P2b Results 2027
- NSCLC | IMMUNOLIFE P2a Interim Analysis Q4 26

#### MaaT034 (co-cultured capsule)

• Solid Tumors IO | Target FIH 26

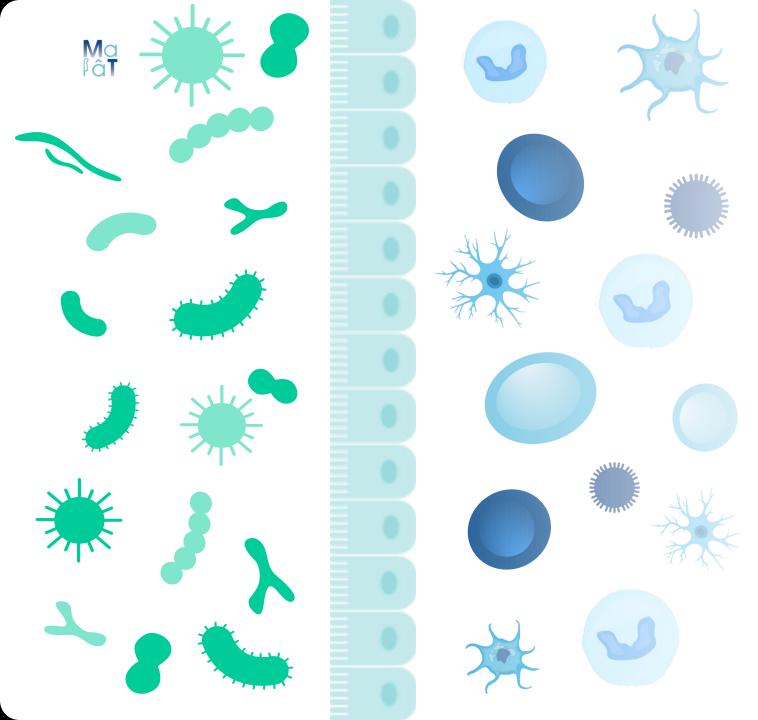
#### MaaTO3X (co-cult. ind.-spec. caps)

• Undisclosed | Next Steps

#### Finance

- Cash position of 27m€ as of September 30, 2024
- Ocash runway into Q2.2025
- Exploring several options to strengthen financing for future developments, including nondilutive and dilutive sources





# Thank you



