



Ma
bâT

MaaT Pharma Microbiota as a Therapy

April 2023

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, tortious, 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).

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.

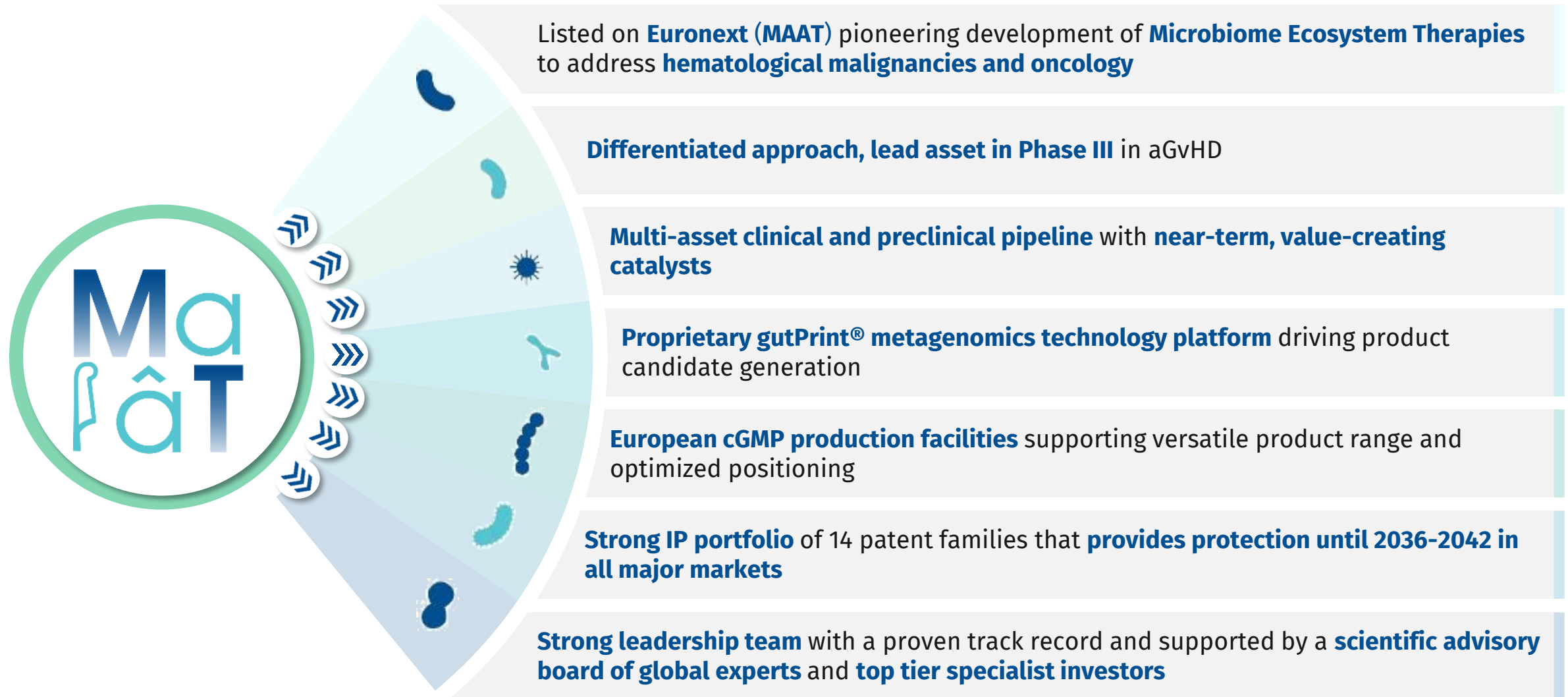
This document contains information on the Company's markets and competitive position, and more specifically, on the size of its markets. This information has been drawn from various sources or from the Company's own estimates which may not be accurate and thus no reliance should be placed on such information. 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.

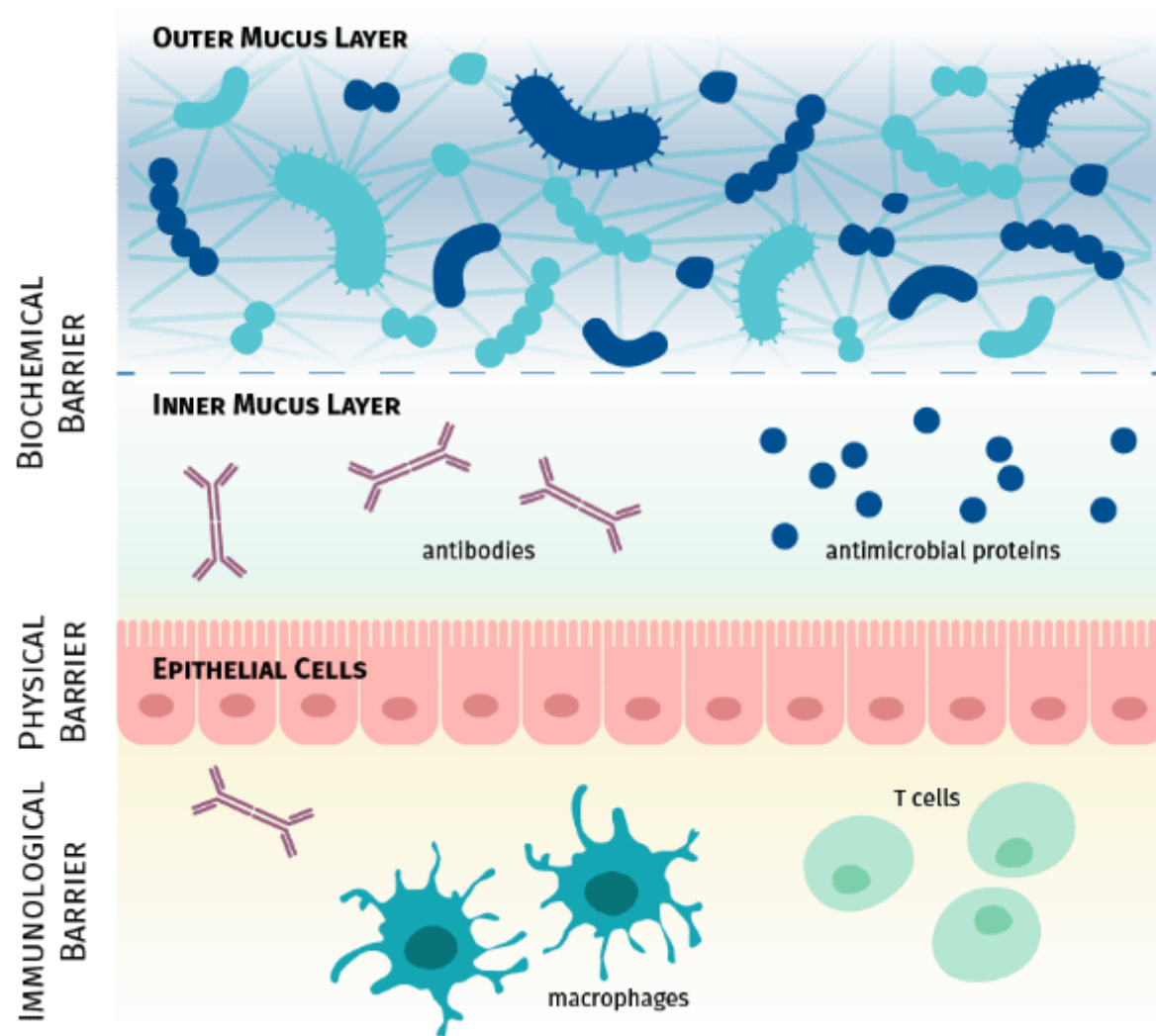
Forward-looking statements are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future. Forward-looking statements cannot, under any circumstance, be construed as a guarantee of the Company's future 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.

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%

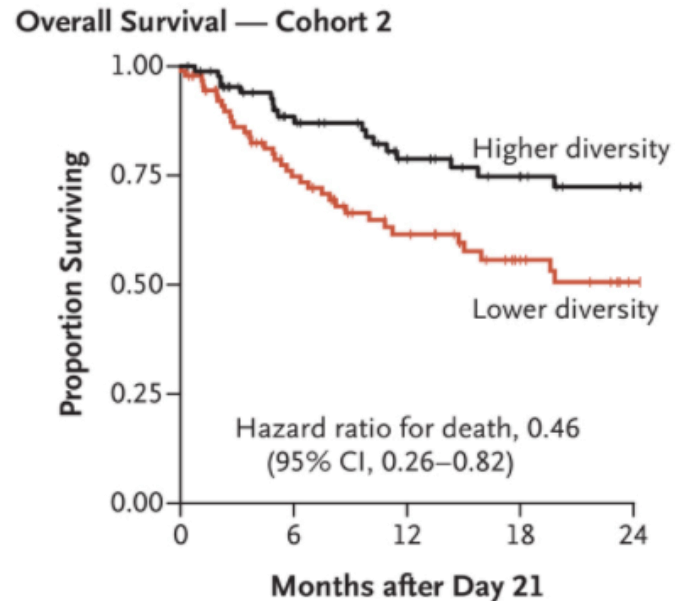
cellular host defense localized in the gut

Diversity matters!

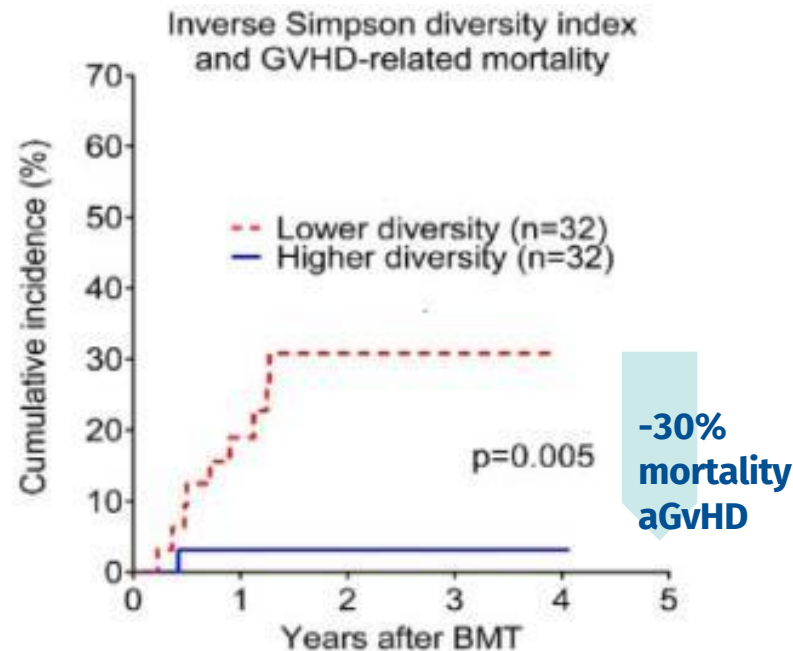
Higher gut microbiome diversity is associated with ...

Liquid Tumors

Higher survival rate in patients receiving allo-HSCT ^{*,1}



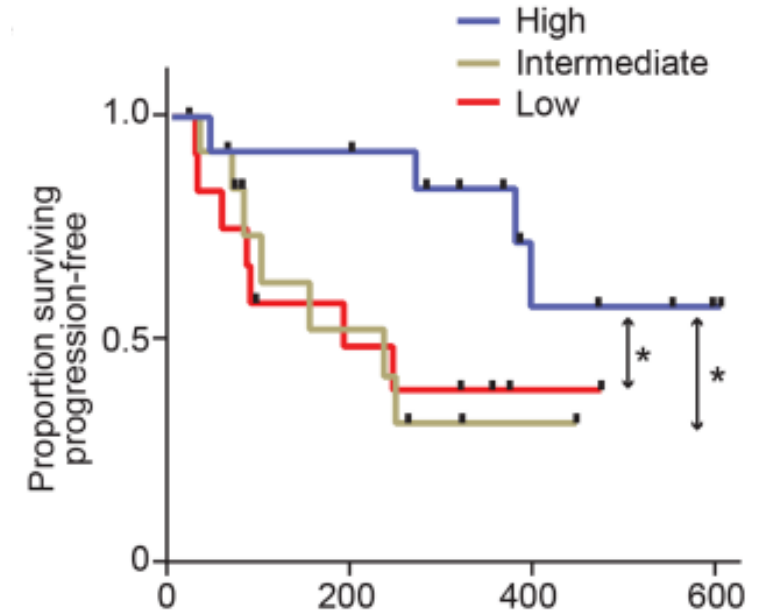
Lower incidence and lower mortality from aGvHD^{*,2}



MaaT Pharma MET Inverse Simpson (mean): 24

Solid Tumors

Higher response rate to ICI* in patients with metastatic melanoma³

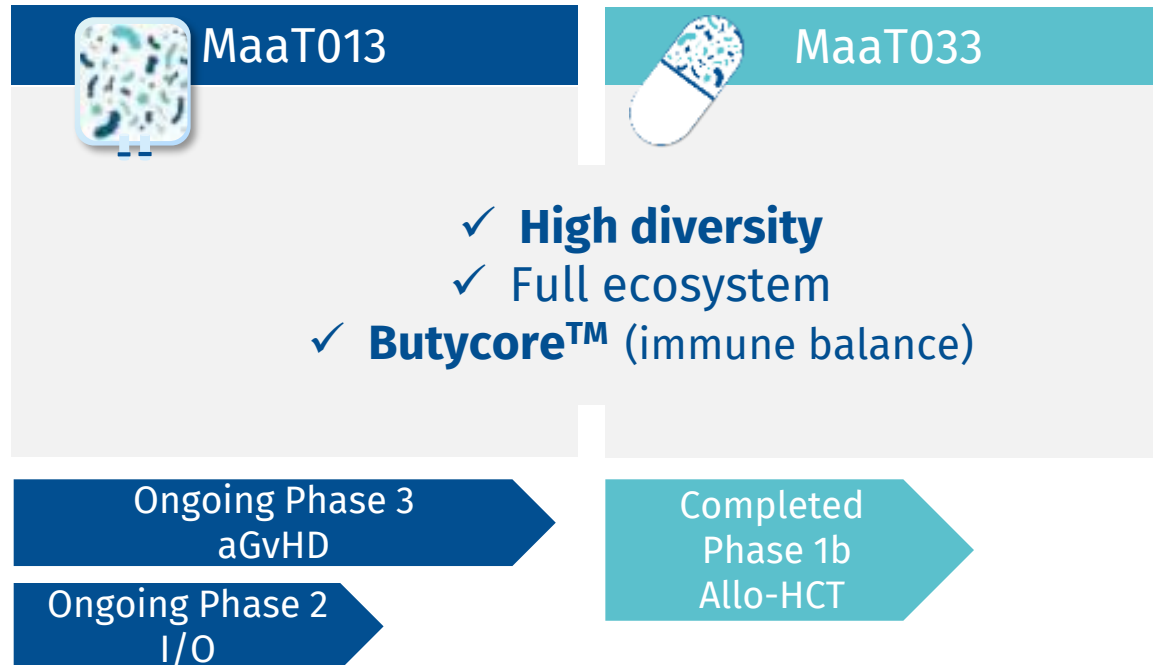


*allo-HSCT: allogeneic hematopoietic stem cell transplantation; aGvHD: acute Graft-vs-host-Disease; ICI: Immune Checkpoint Inhibitors
¹Peled, J.U. & al N Engl J Med 2020;382:822-34; ²Ghani, 2021; Jenq RR. et al, Biol Blood Marrow Transplant 21 (2015) 1373e1383; Pamer, Blood, 2014 ; ³Gopalakrishnan et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

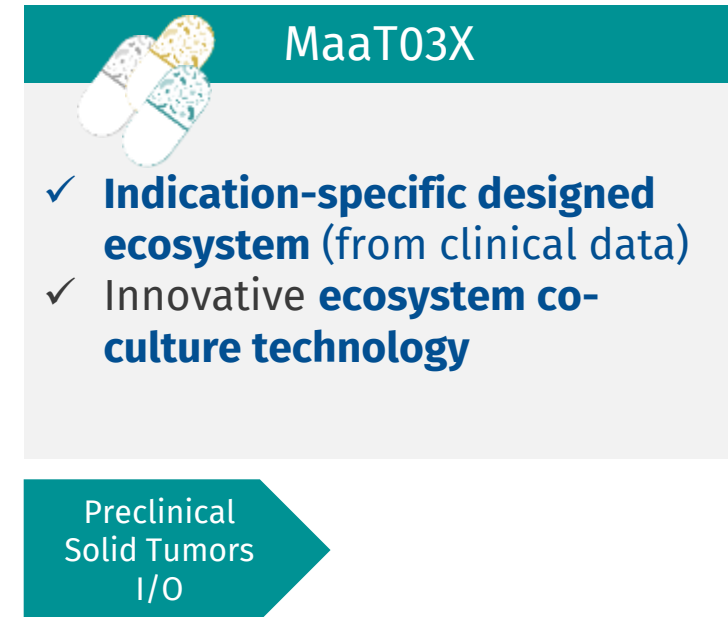
MaaT Pharma's Microbiome Ecosystem Therapy (MET) platform has generated a diverse line of product candidates



Native

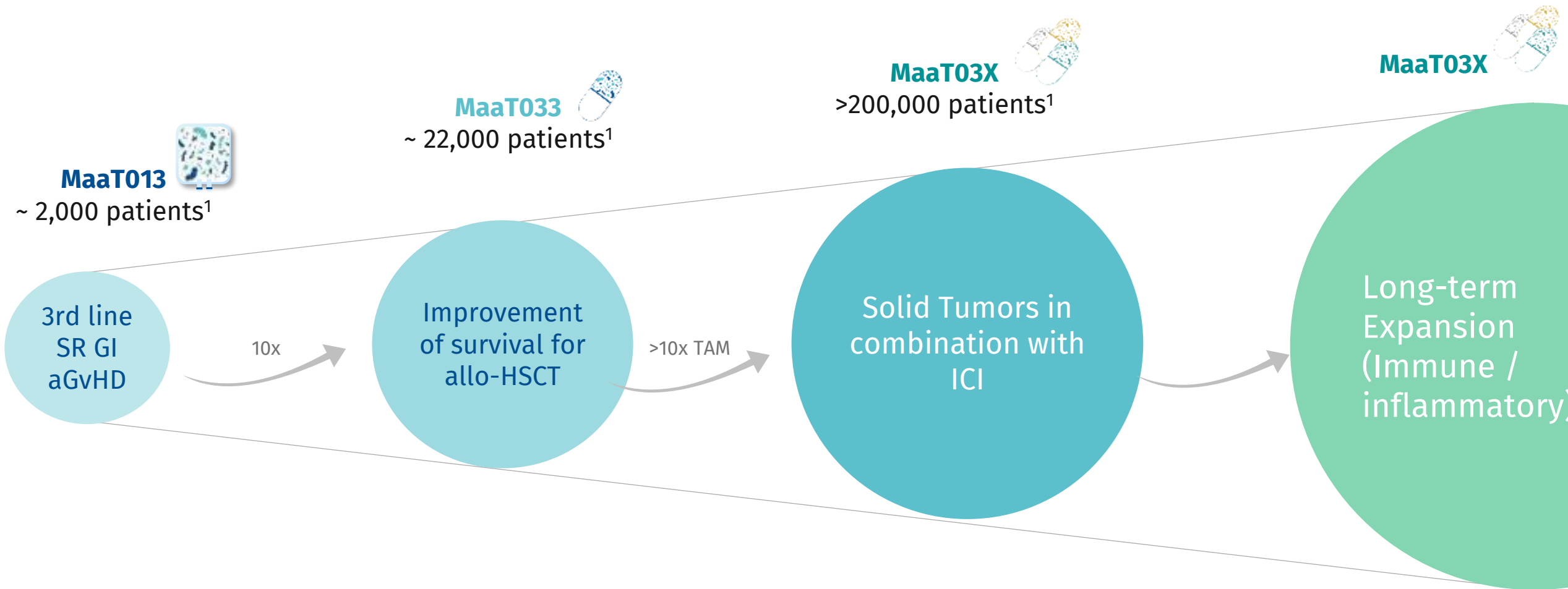


Co-cultured

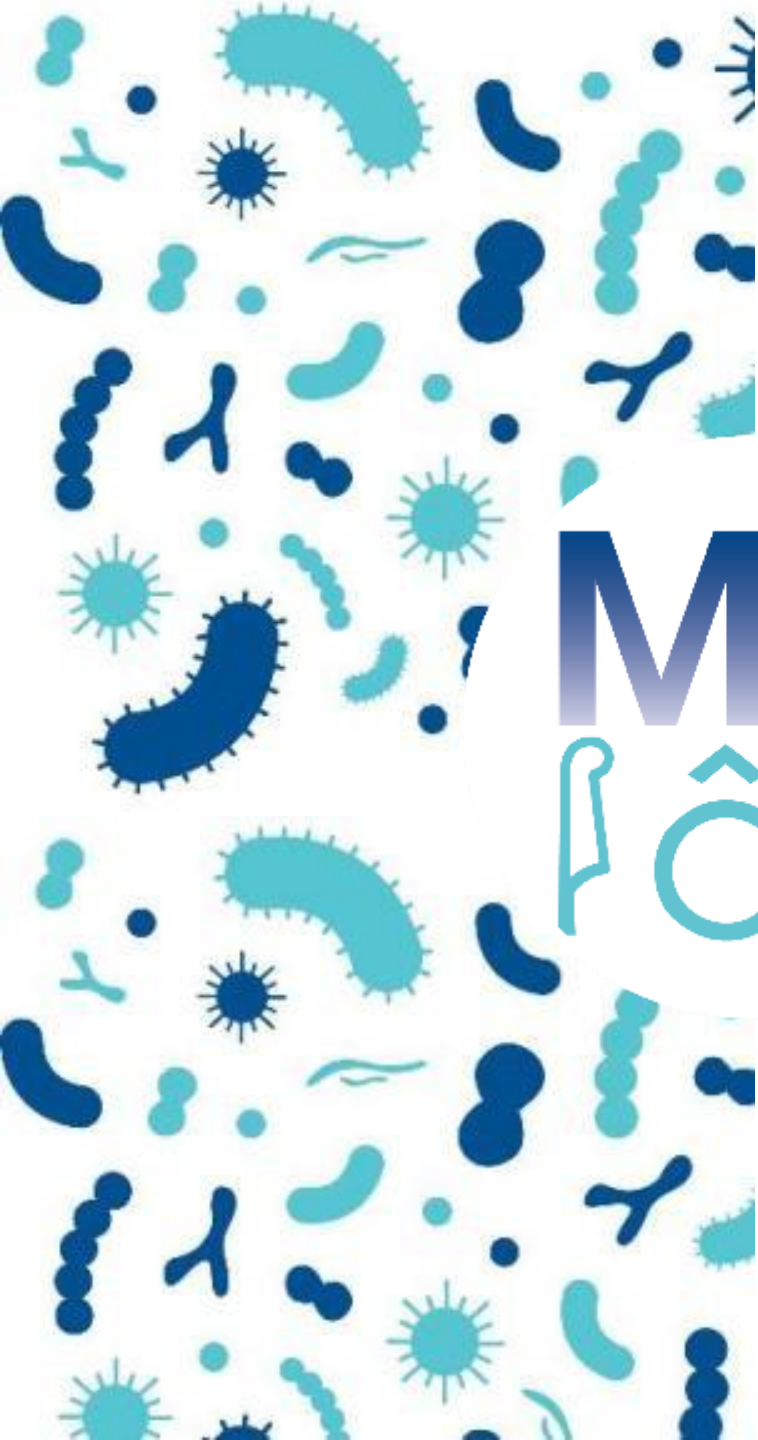


¹ **Butycore™**: Group of 15 different genera known to produce short-chain fatty acids with anti-inflammatory properties

Looking ahead: addressing growing market opportunities with severe medical need



¹ EU5, US, and Japan

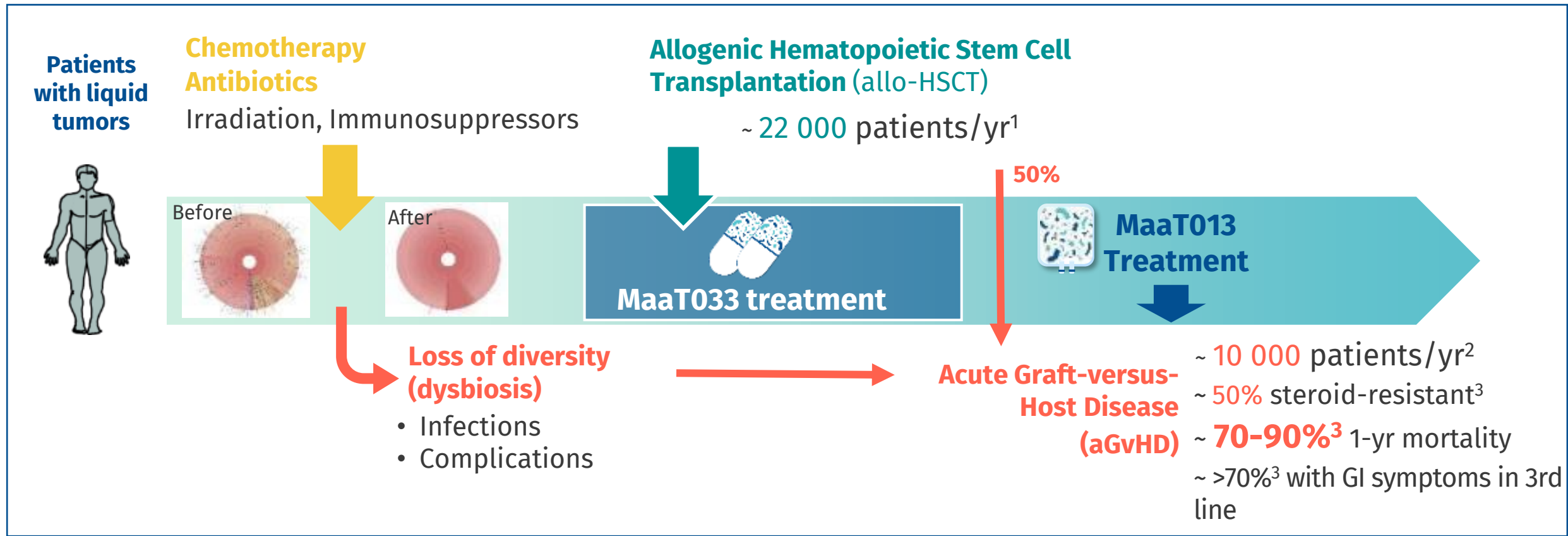


Ma bệnh

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, ³ According to MAGIC database

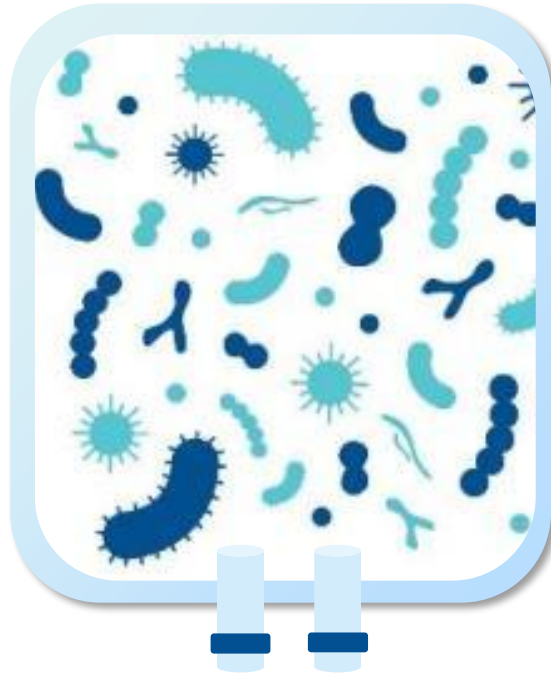


Hemato-Oncology
Liquid Tumors

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

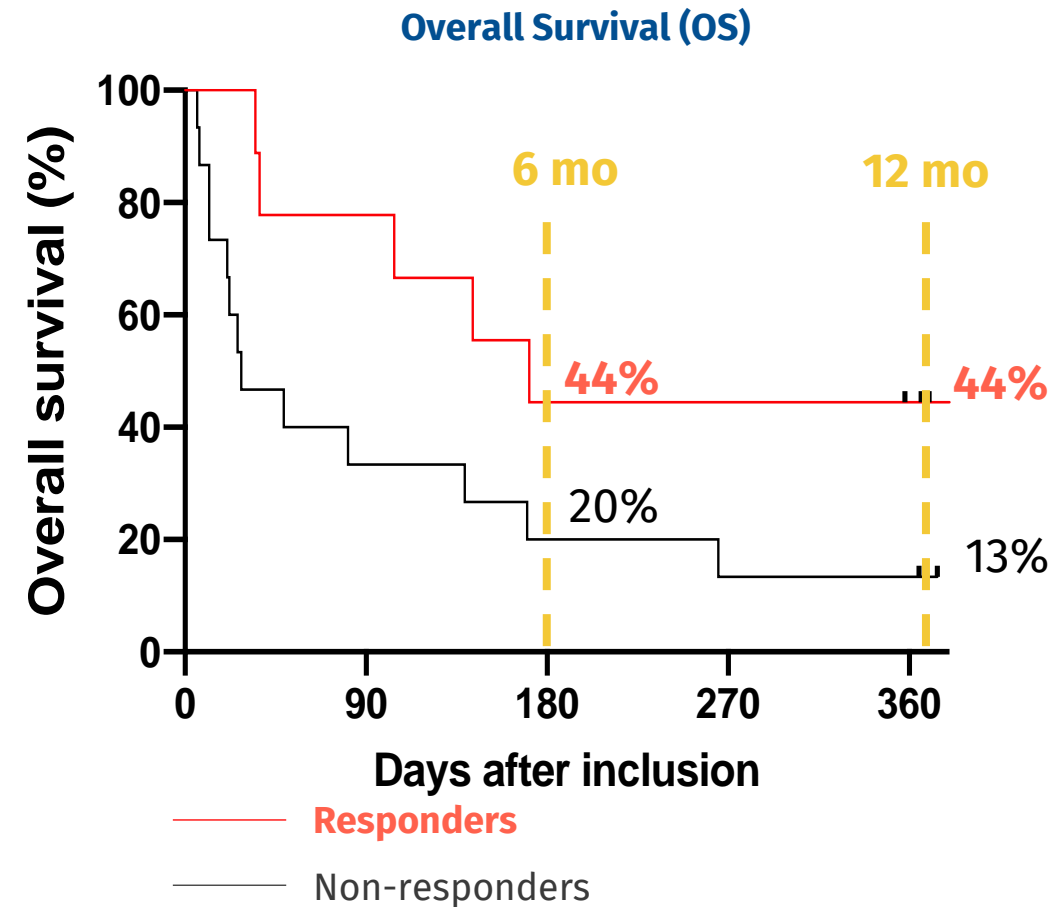
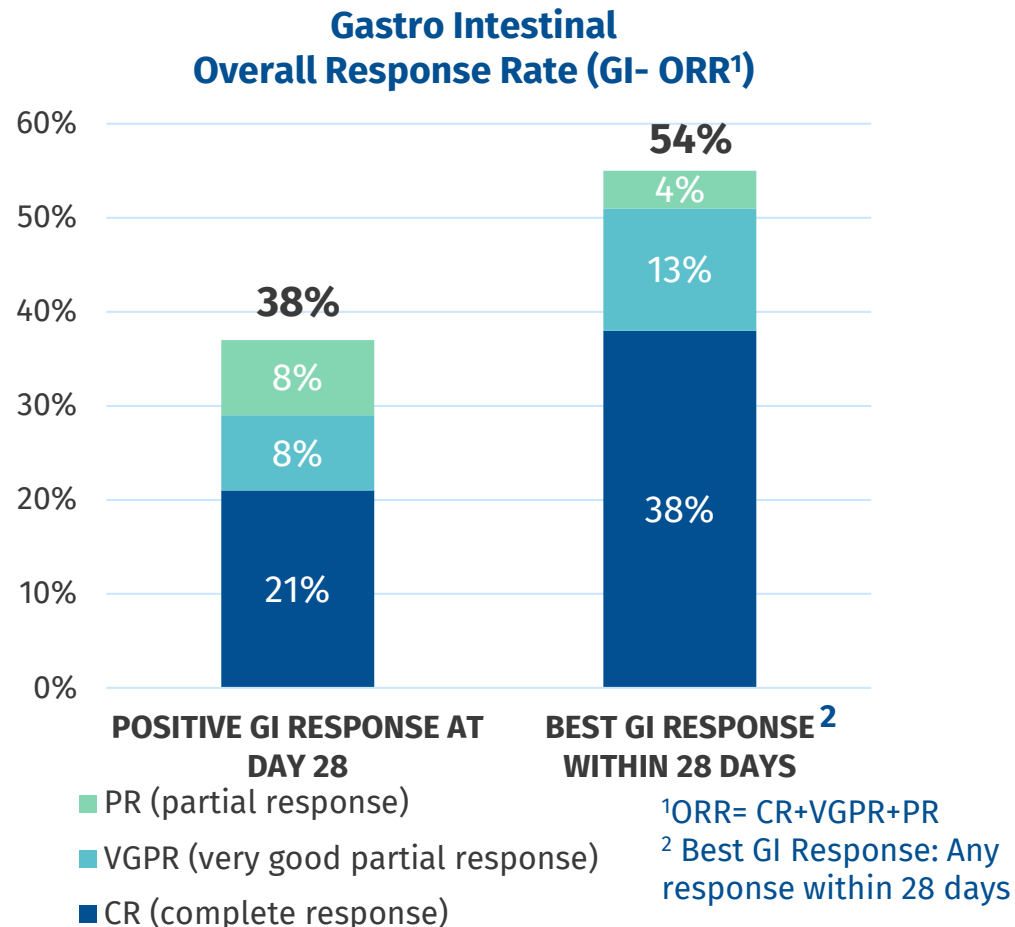
MaaT013 has received Orphan Drug Designation from FDA and EMA



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), 2nd line (Steroid-resistant)
- Very good safety and tolerability profile
- MaaT013 increases responders' gut microbiome diversity

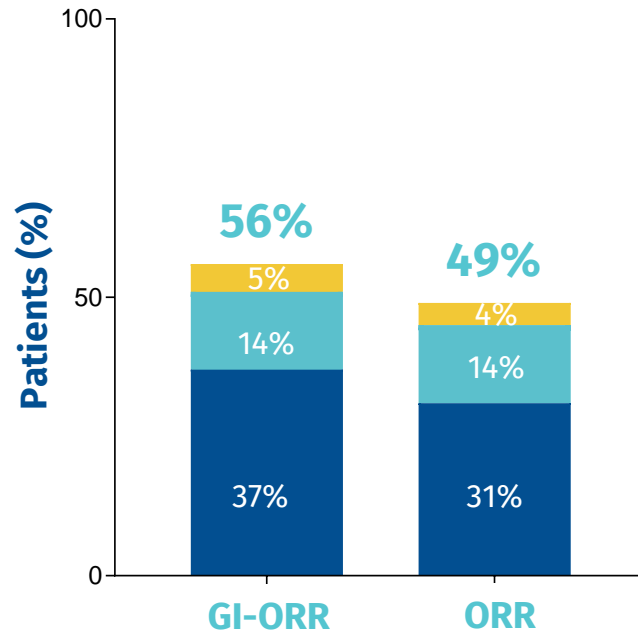




Early Access Program (EAP) is corroborating positive data in an advanced, severe and more diverse GI aGvHD population

- 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 64th Annual Meeting of the American Society of Hematology (ASH)

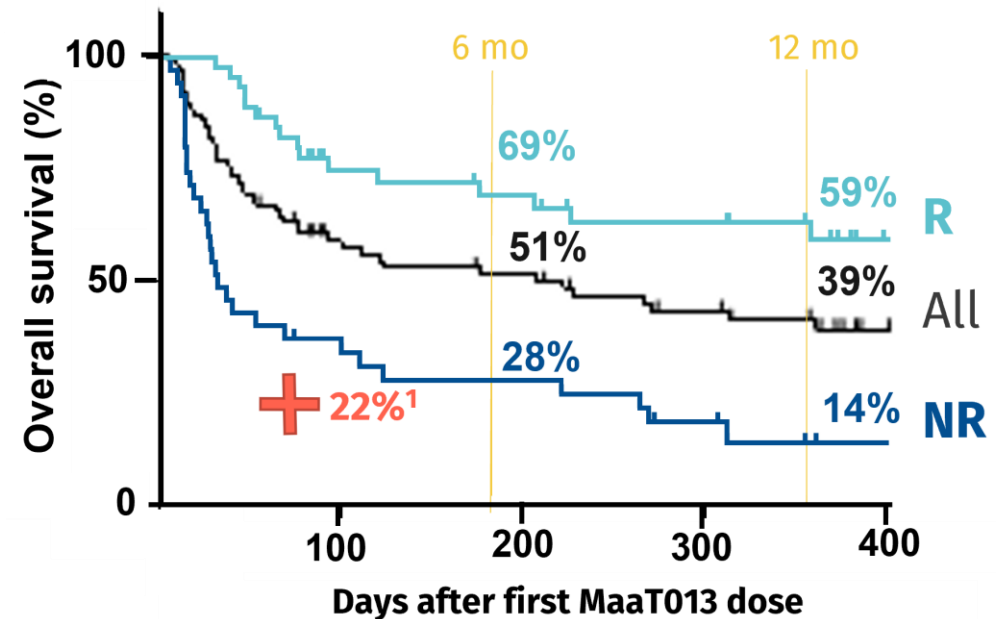
**Gastro Intestinal
Overall Response Rate (GI- ORR¹)**



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

¹ORR= CR+VGPR+PR

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



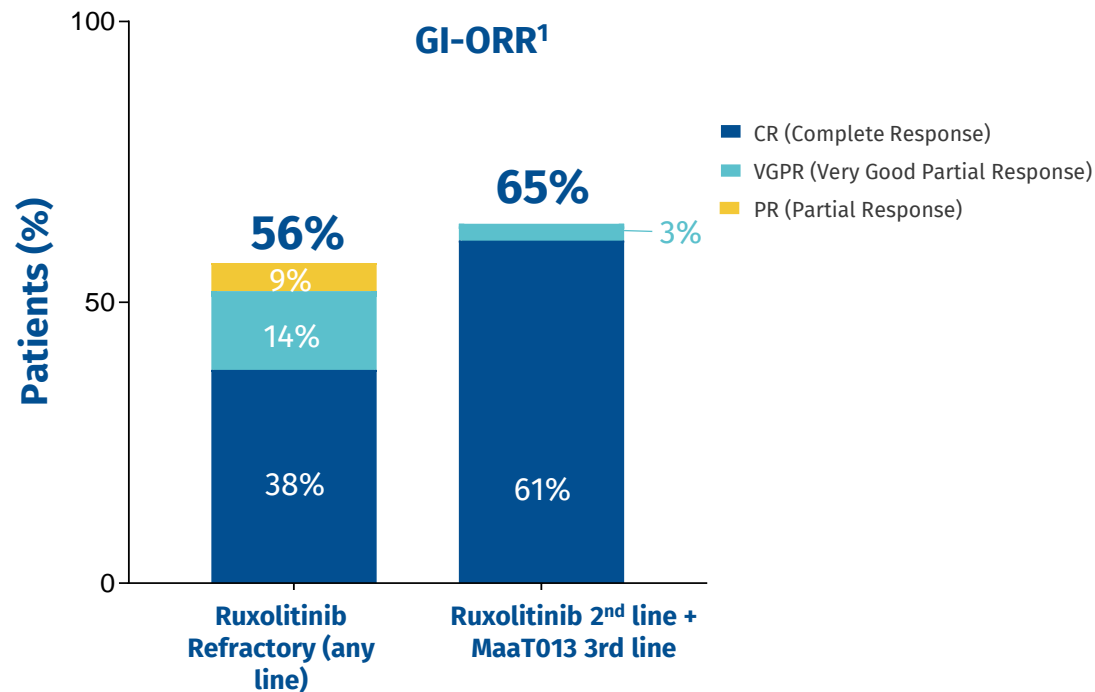
¹OS expected in ruxolitinib-resistant patients at 2 months (REACH1 study)

*(MAGIC Classification)



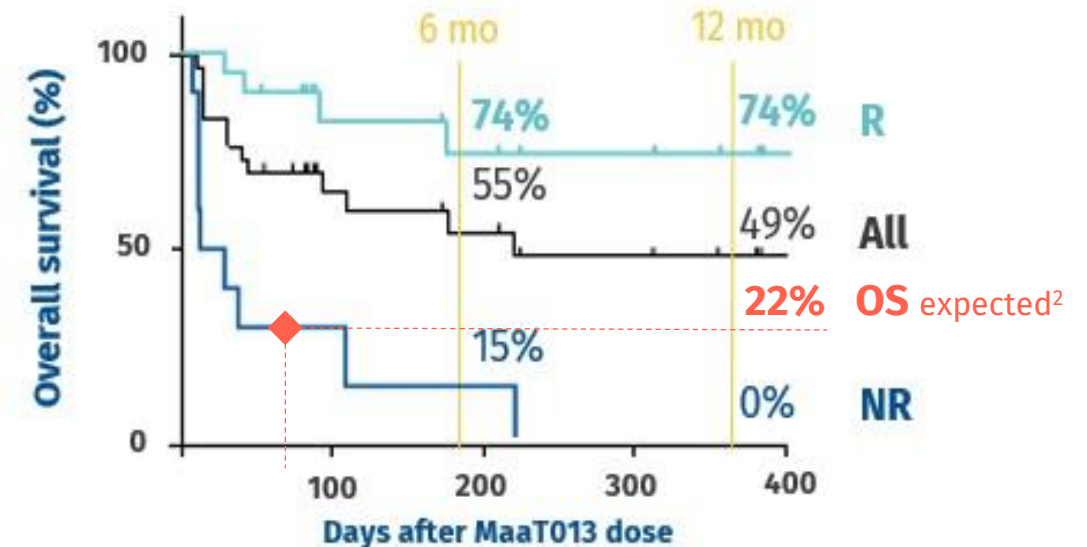
Among 81 patients in EAP, excellent response to MaaT013 was shown in n=31 corticoid and ruxolitinib-refractory patients

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



¹ORR= CR+VGPR+PR

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



²OS 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 3rd line agent in GI aGvHD treatment

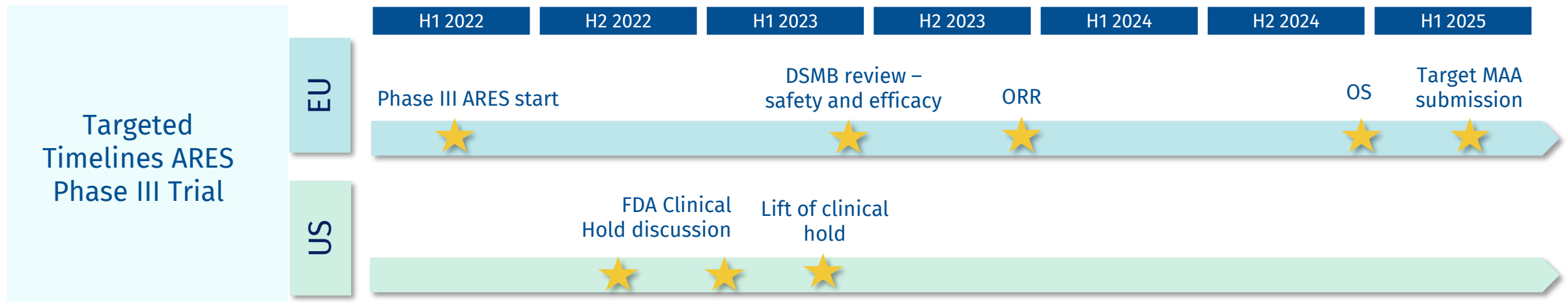
- Further investigation currently ongoing in a pivotal single arm Phase 3 trial of MaaT013 as 3rd line
- 75 patients with GI aGvHD who are refractory to both steroids and ruxolitinib
- Primary endpoint: GI-ORR at Day28
- The Company continues the late-stage clinical development of MaaT013 in Europe

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.



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

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



Hemato-Oncology
Liquid Tumors

Improving survival in allogeneic Hematopoietic
Stem Cell Transplantation patients



MaaT033: An oral capsule to be used as an *adjunctive and maintenance 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 Ph1b: Dose-finding study (completed)
- Planning **Phase 2b trial** to evaluate MaaT033 to improve overall survival in allo-HSCT patients

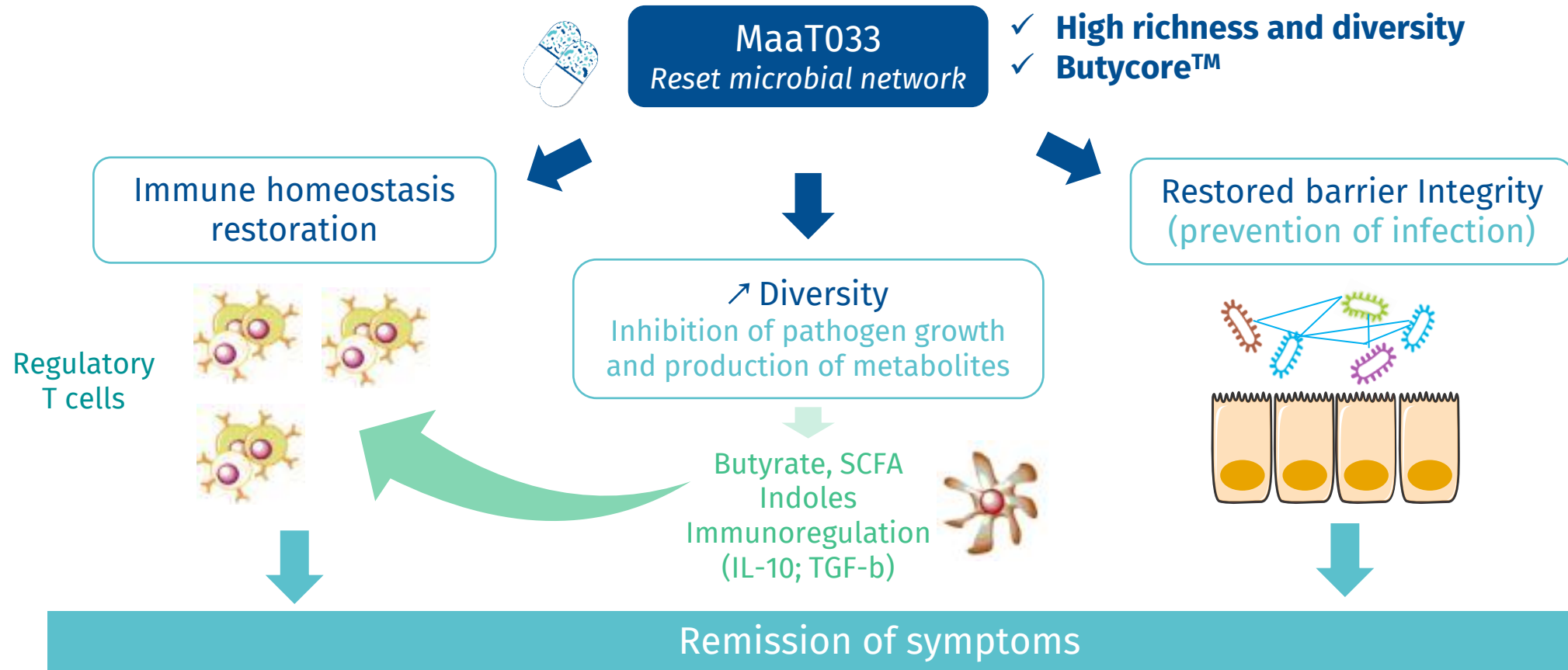


Indication

To improve survival of allo-HSCT patients



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



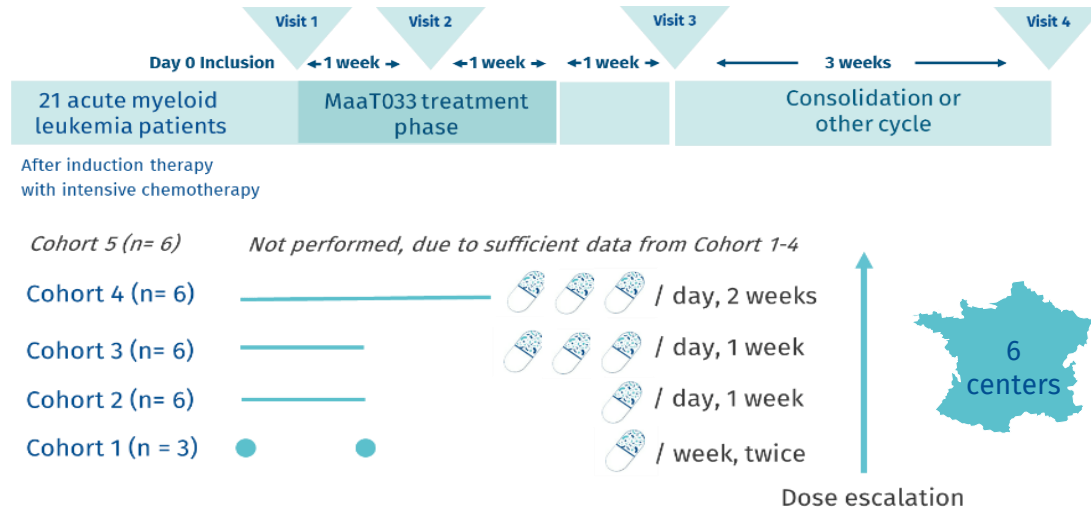
AML
Phase 1



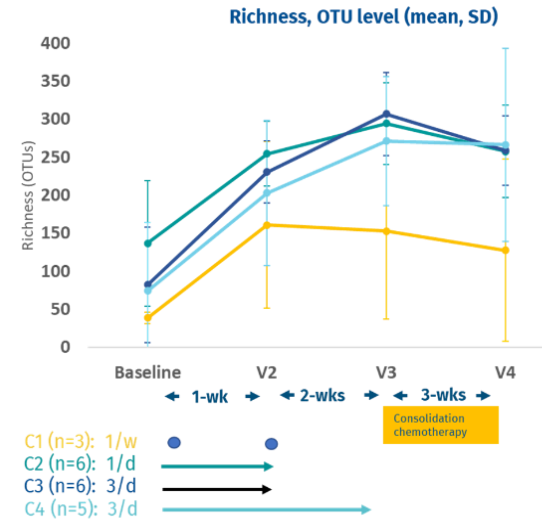
Data presented
at ASH 2022



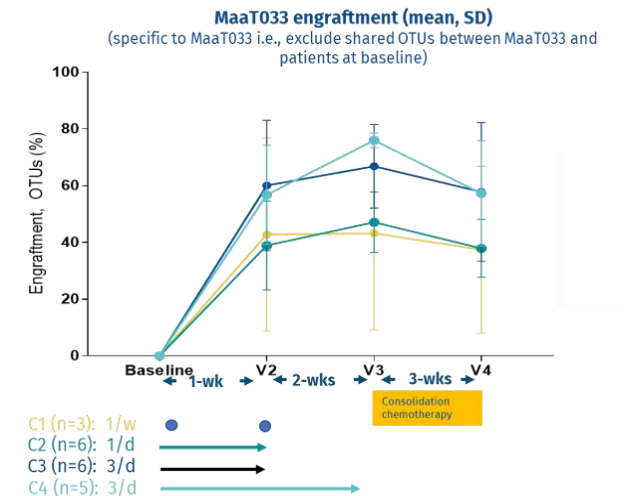
Phase Ib study aimed to determine MaaT033 dose for further clinical development



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.

→ Dose selected for planned Phase 2b study
→ Study expected to initiate in Q2 2023



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



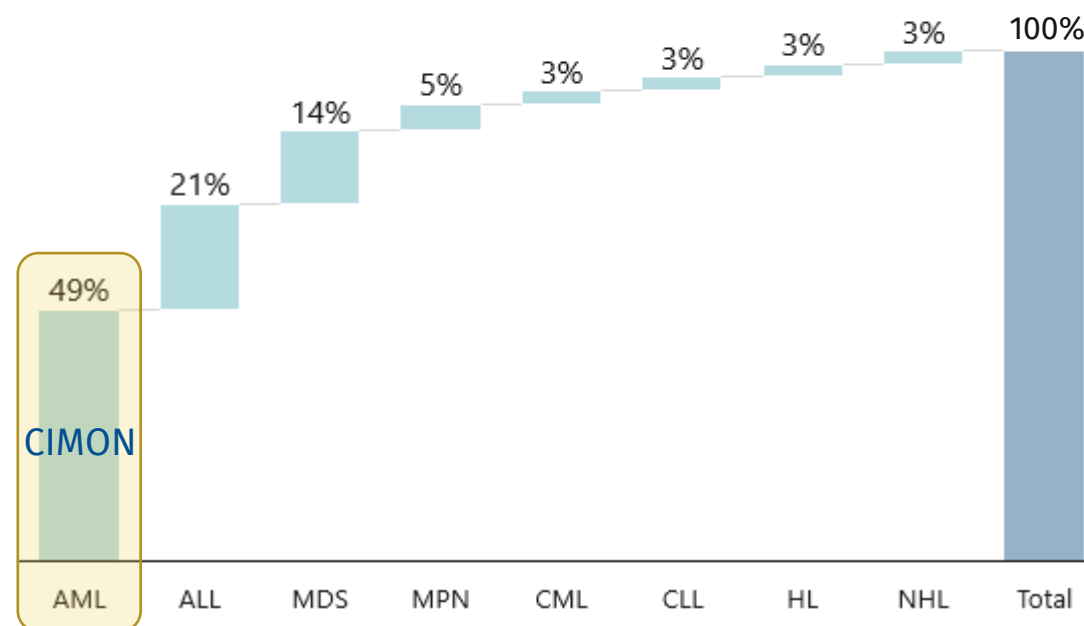
Japan

c. 3,000
primary
procedures

Additional 7%-10% recurrent procedures

Approximately 22,500 procedures/year

Hematological Malignancy Patients Receiving Allo-HSCT¹

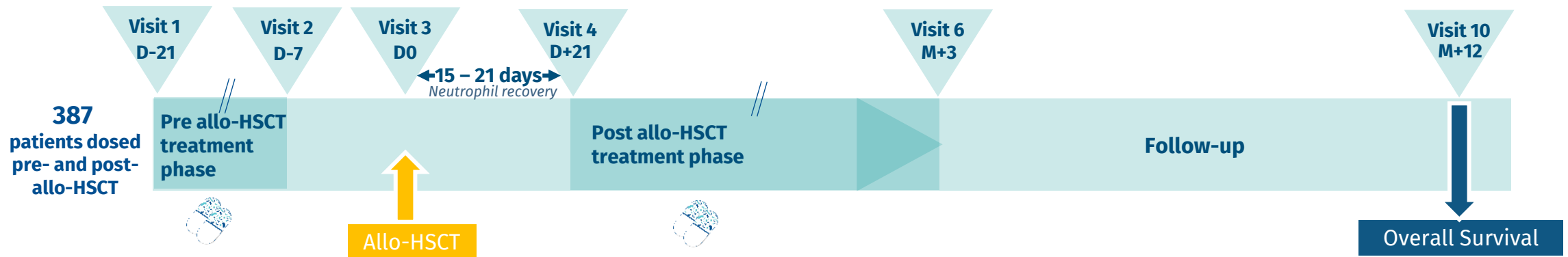


AML : acute myeloid leukemia; ALL : acute lymphoblastic leukemia ; MDS : myelodysplastic syndrome; MPN : myeloproliferative neoplasms ; CML: chronic myeloid leukemia ; CLL : chronic lymphocytic leukemia ; HL: Hodgkin's Lymphoma ; NHL: Non Hodgkin Lymphoma

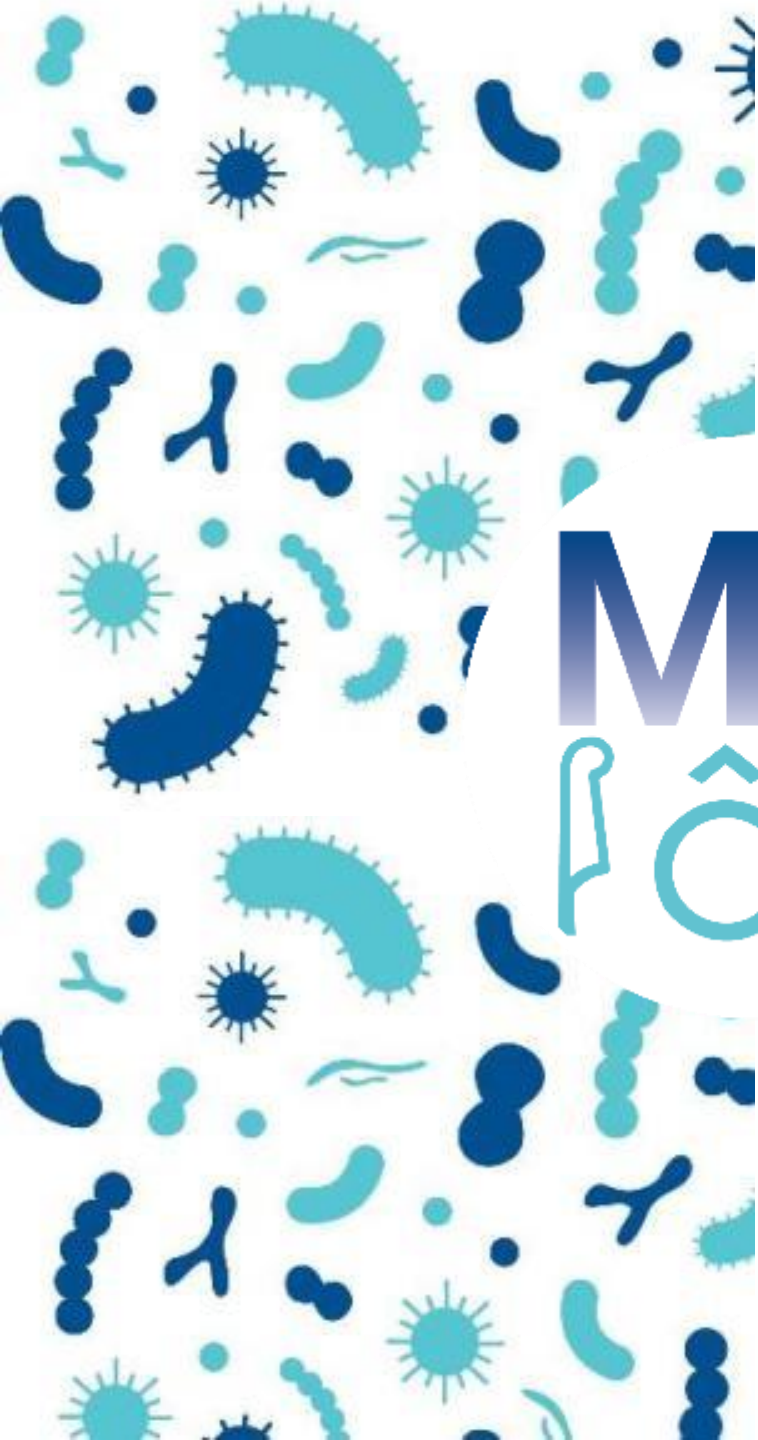
¹EBMT aHSCT Survey, 2017 (published in Bone Marrow Transplantation (2019) 54:1575–1585), Global Data 2020

The Phase 2b is designed to establish MaaT033 *as an adjunctive and maintenance 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 H1 2023, results are expected in H1 2026



¹Expansion to US sites subject to ongoing discussion with the FDA for MaaT013 IND;



Ma
bắt

Immuno-Oncology
Solid Tumors

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

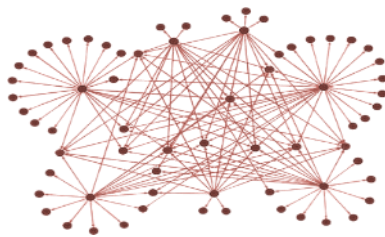
FMT from ICI responders to ICI non-responding patients with metastatic melanoma

✓ **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^{1,2,3,4}
- FMT from ICI responders (R) could induce response in metastatic melanoma non-responders (NR)^{5,6}

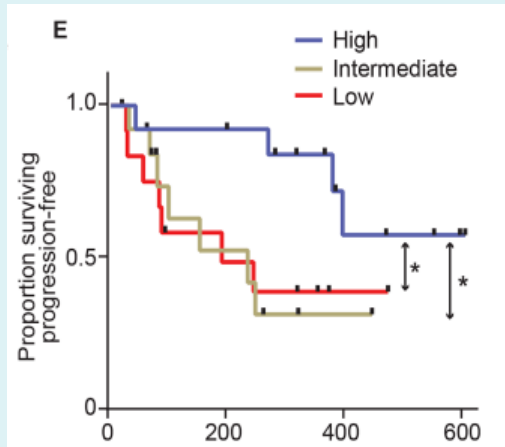
→ Leveraging the gut microbiome richness, diversity and its key functional networks may be a game-changer in immuno-oncology in the coming years

¹. Gopalakrishnan et al, Science 2018; ². Matson, et al Science 2018; ³. Routy et al, Science 2017;

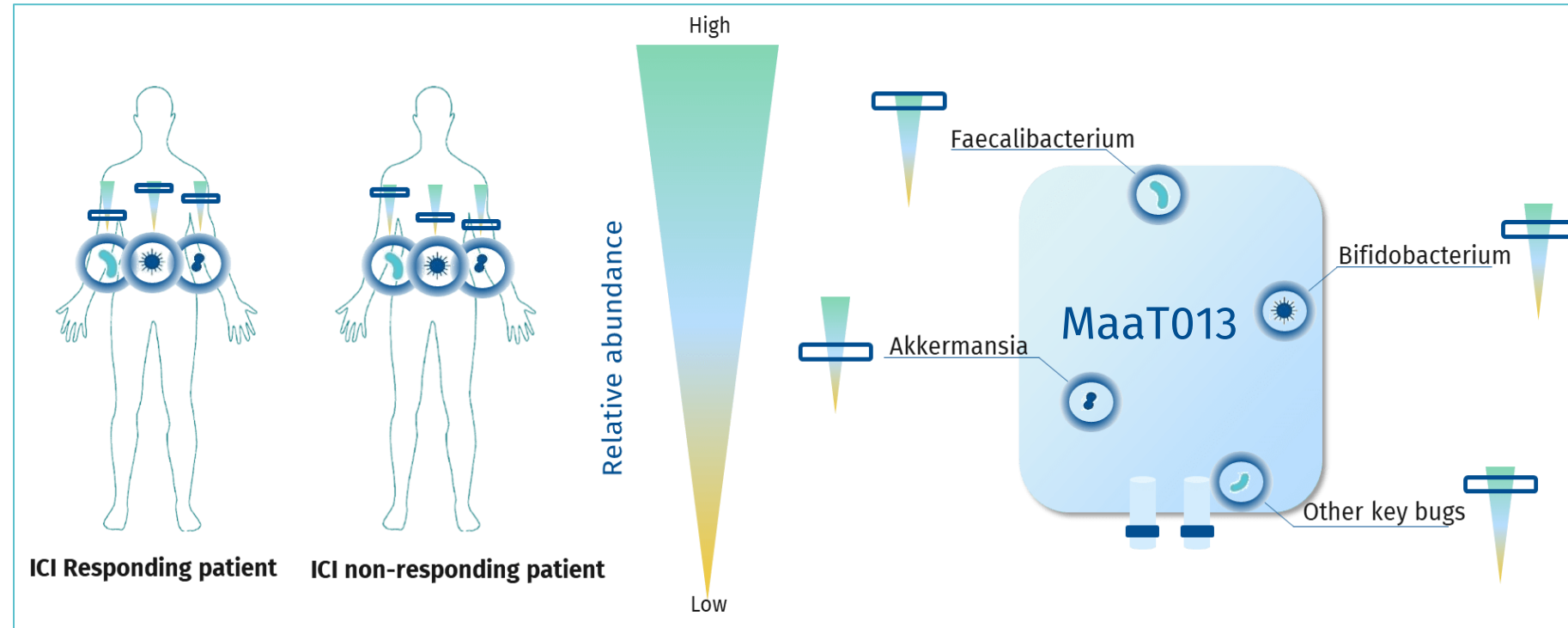
⁴. Mc Culloch et al, Nat Med 2022; ⁵. Baruch et al, Science 2021; ⁶. Davar et al, Science 2021

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

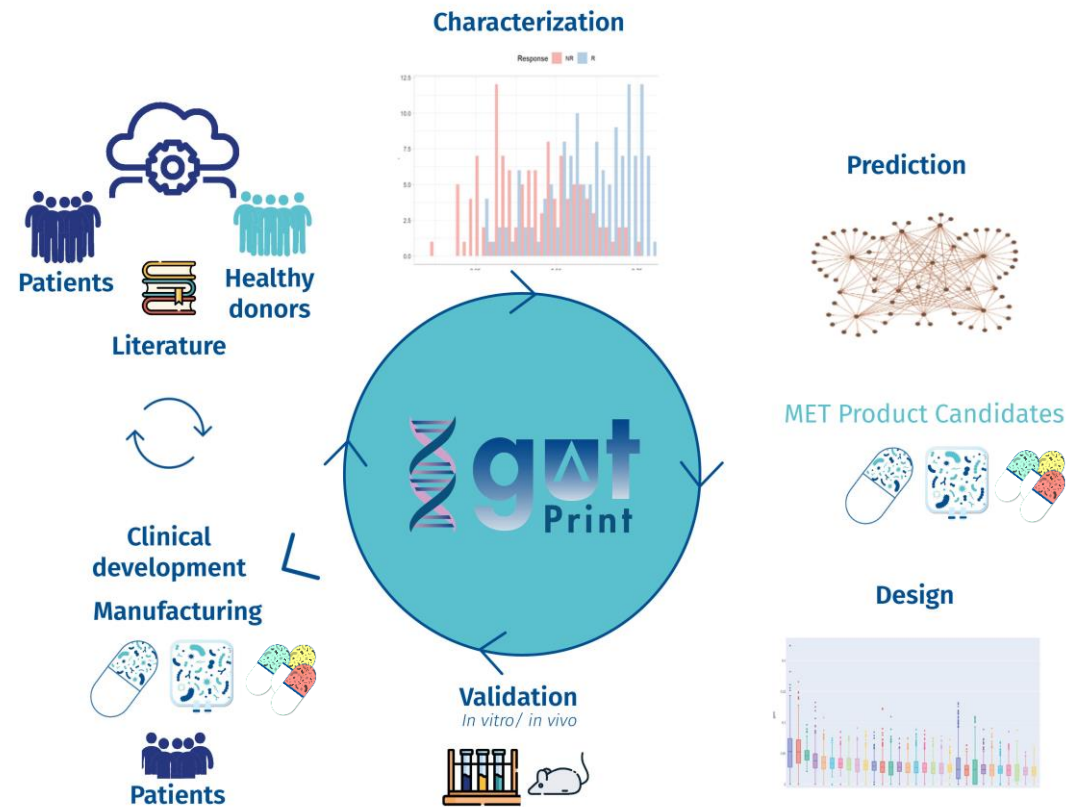


Ongoing Phase IIa PICASSO trial¹, in collaboration with **Assistance Publique - Hôpitaux de Paris** (sponsor).

- ✓ **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

¹ Registered trial #NCT04988841

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



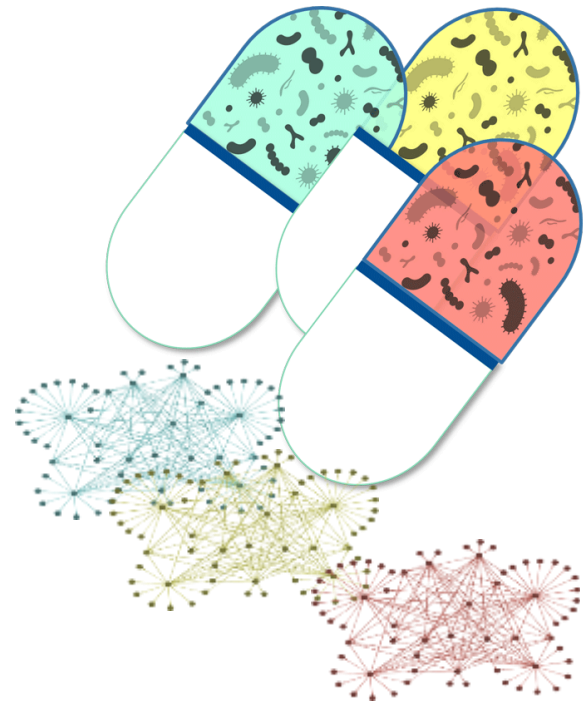
gutPrint® is the engine that drives MaaT Pharma's MET product candidate generation capabilities to broaden and strengthen the pipeline

- ✓ 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

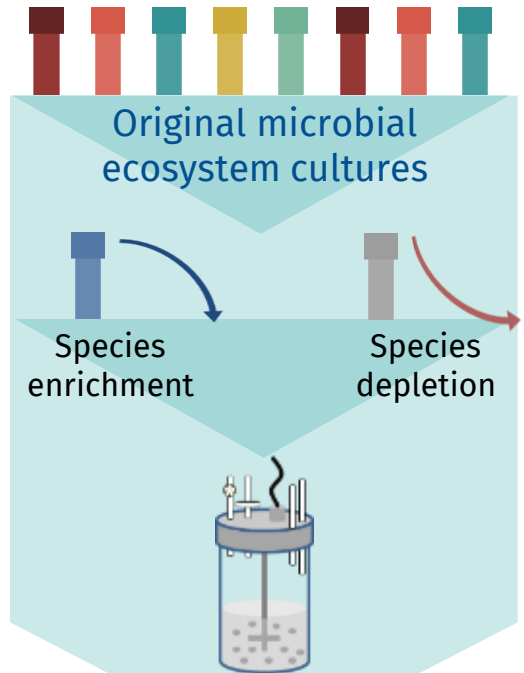
- ✓ First candidate in preclinical development
- Targeting FIH H1 2024



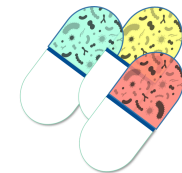
Indication

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

Customizable, donor-independent, scalable co-culture process



CO-CULTURED A FULL ECOSYSTEM



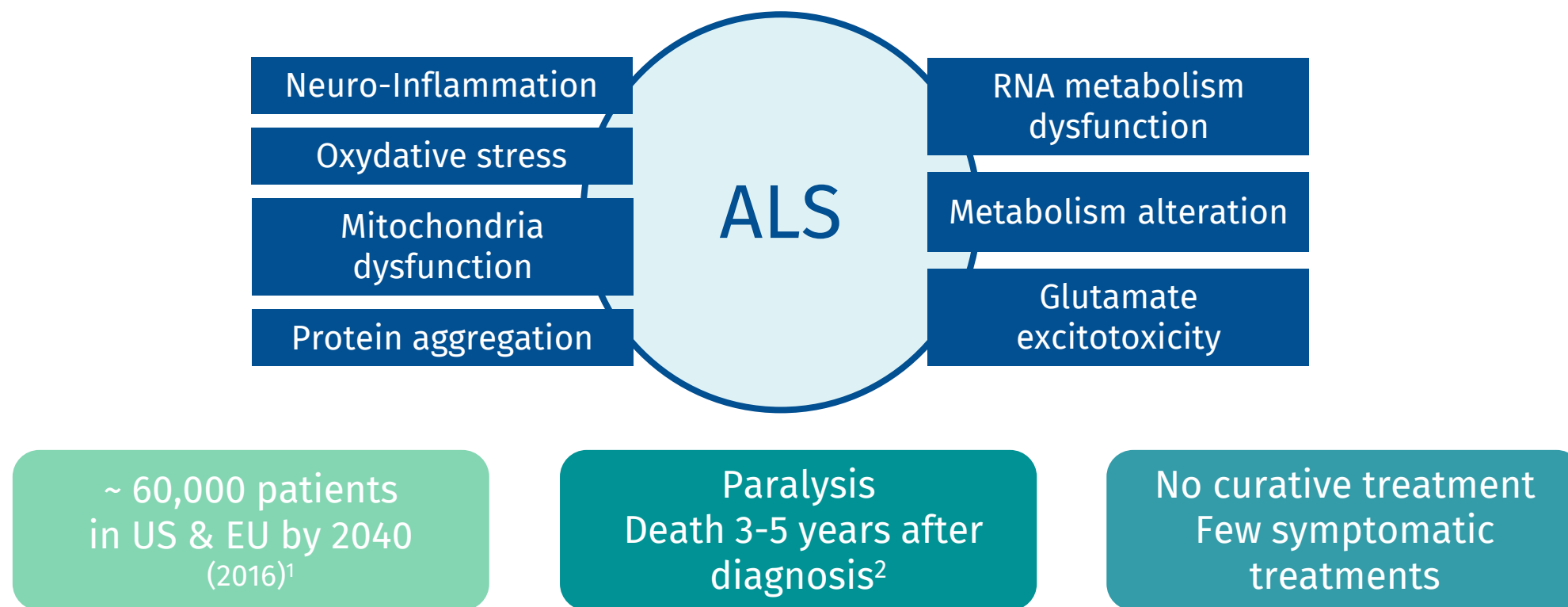


Ma
bât

Neuro-degenerative diseases:
Amyotrophic Lateral Sclerosis
(ALS)



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



¹Arthur, 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>

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



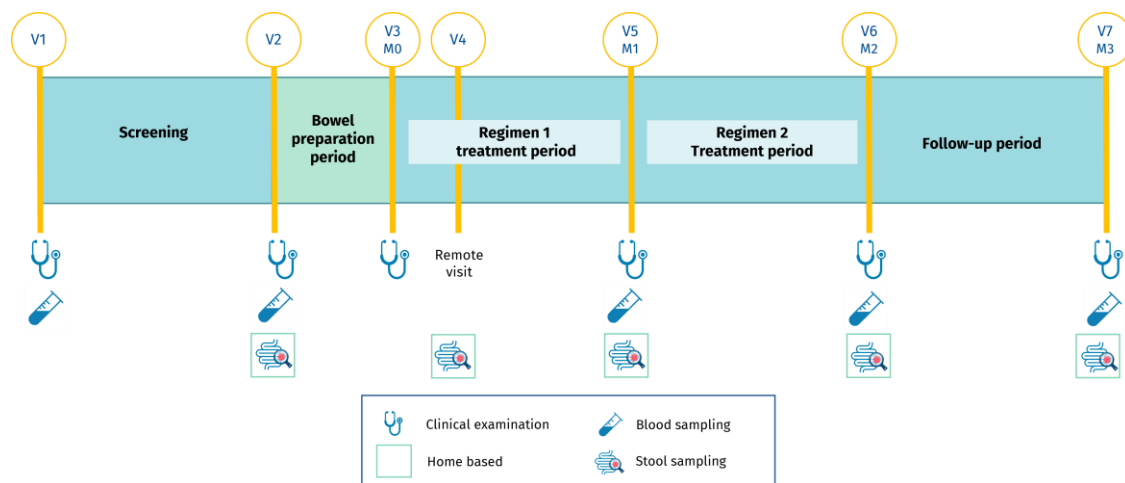
IASO trial is designed to develop the potential first oral microbiotherapy in ALS*

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



Ma
phát

End-to-End in-house cGMP
manufacturing

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



Building a dedicated 1,600m² 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.



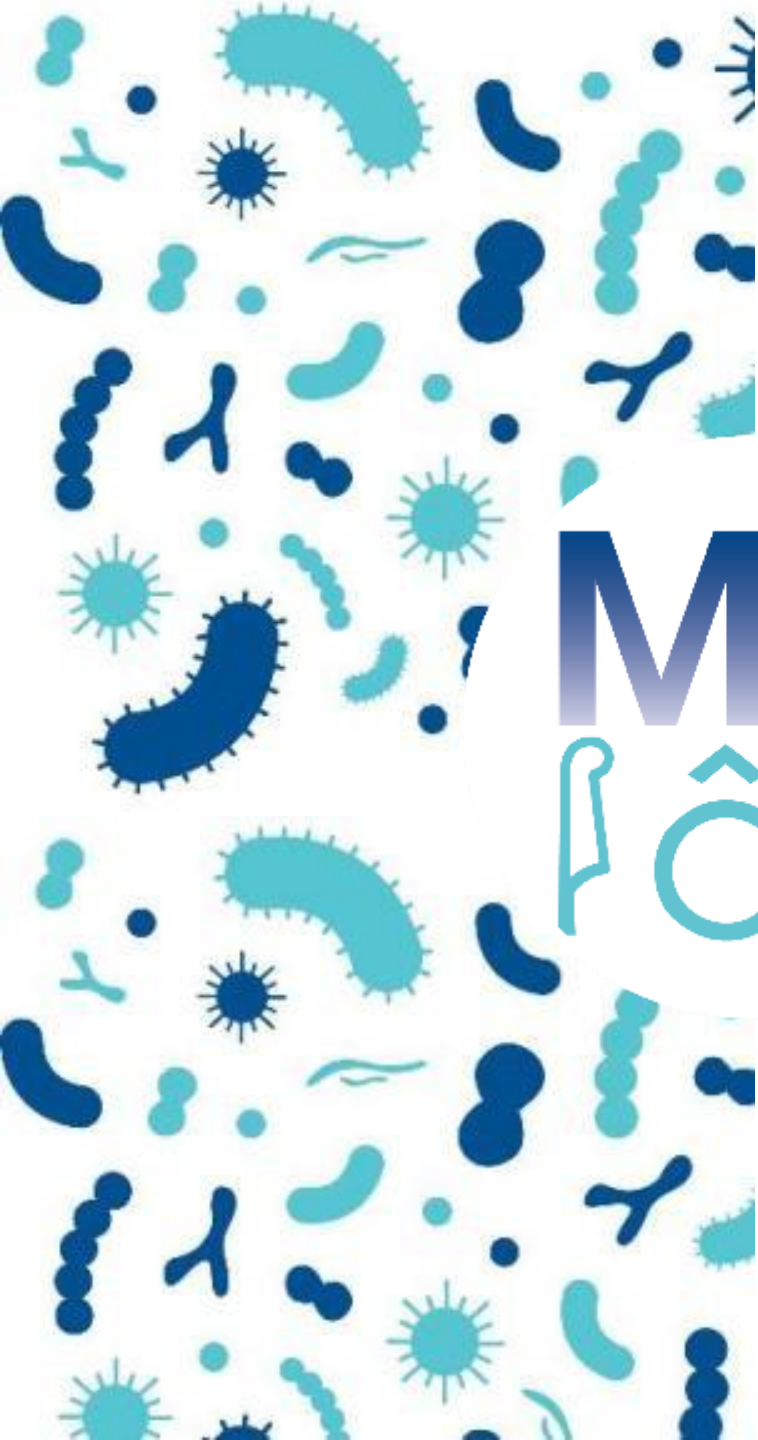
Ongoing CSR global strategy: participating in a reforestation program in France (opting for more ecological items (GoGreen) and joining the Cap Vert pour la forêt program and furnishing the plant with sustainable & used materials

Partnership with  Skyepharma



Artist's representation of future plant

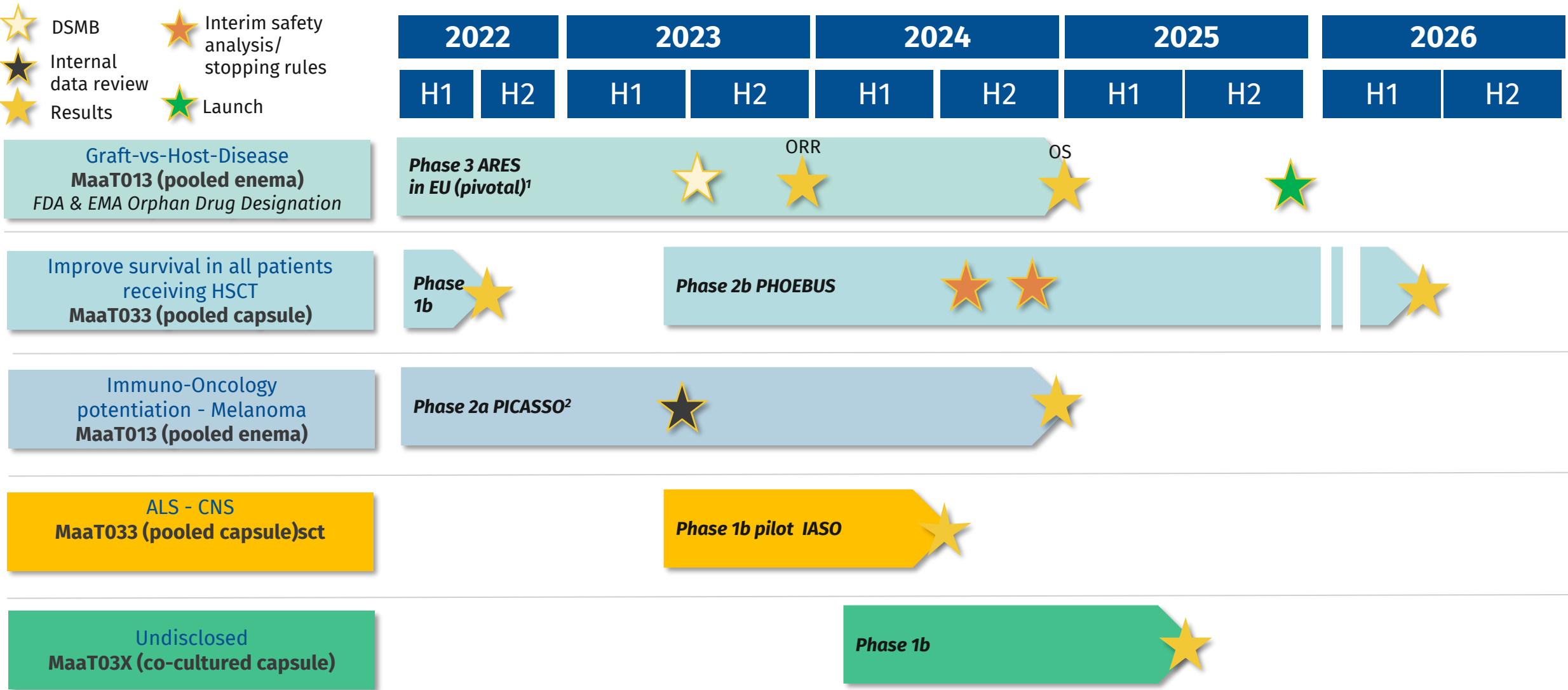
Delivery expected in mid-2023



Mã
bắt

Upcoming key milestones

Meaningful milestones in both the near and long term



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



Siân Crouzet
Chief Operating Officer/
Chief Financial Officer



Carole Schwintner, Ph.D
Chief Technology Officer



Savita Bernal, Ph.D
Chief Business Officer



Isabelle Adeline, Ph.D
Chief of staff



Nathalie Corvaia, Ph.D
Chief Scientific Officer



Pierre Fabre



Jean-Marie Lefèvre
Chairman & 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

BOARD OF DIRECTORS

* 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.

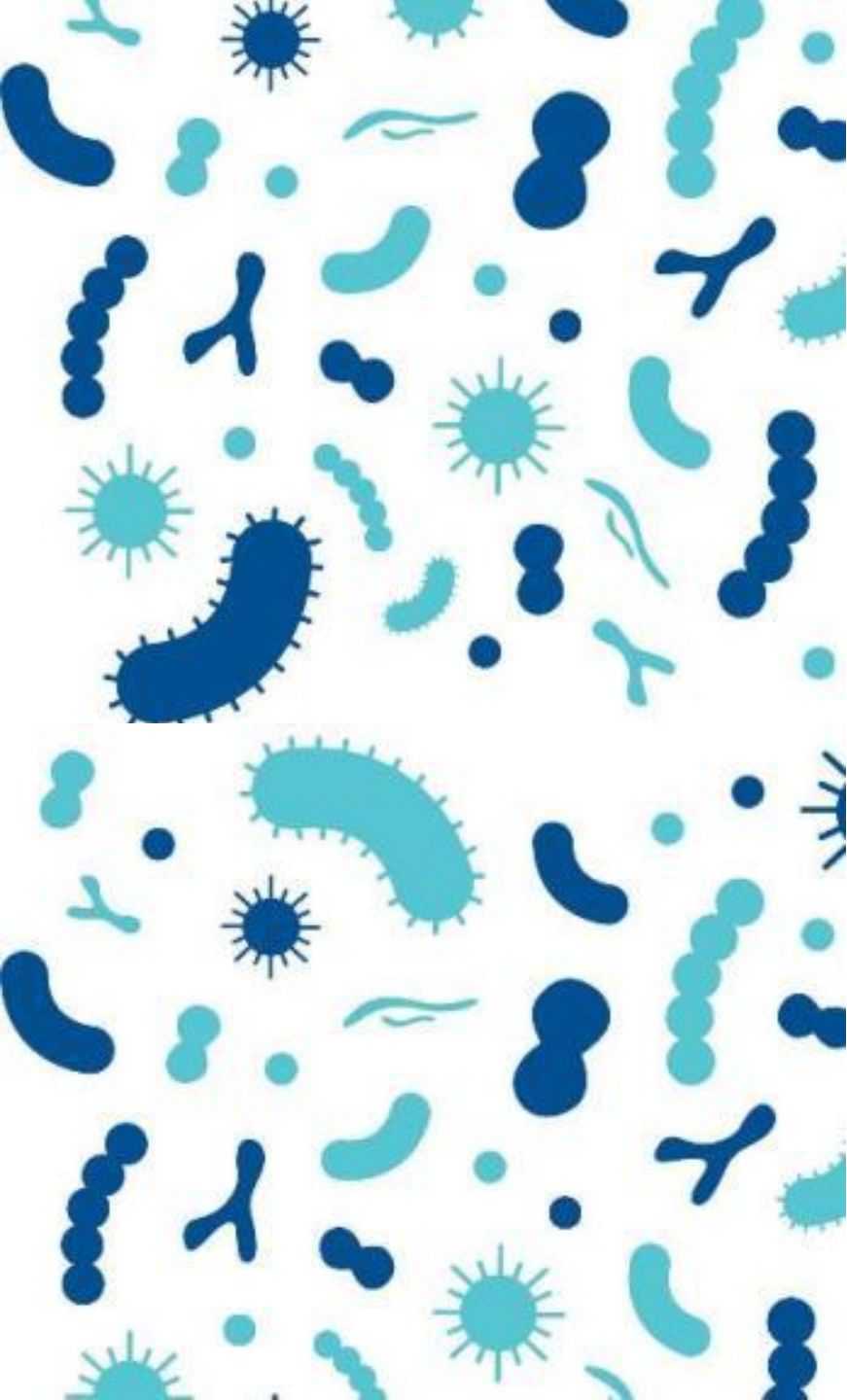
Patients are our priority. We are committed to our patients and to the protection of human health by respecting environmental protection, respecting our employees and ensuring good governance practices. Our way of working every day is driven by the 4 guidelines below:

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



THANK
YOU