15 de noviembre de 2022

Liposome-based Biomimetic Therapy Platform for autoimmune diseases

AHEAD THERAPEUTICS

Martí Dalmases

Content

Therapeutics' Aim

We offer them **something beyond today's palliative treatment** that has secondary effects.

We offer them an **OPTION FOR HEALING.**

We want to **change the lives** of people diagnosed with **autoimmune diseases.**

We want to **reduce their suffering** and **MODIFY the disease course.**

Ahead Therapeutics in a Nutshell

The only platform showing proven biomimetic treatments involving **T-reg** pathway

2 lead assets with promising results ready to be pushed towards clinical studies

- **Rheumatoid Arthritis**
- **Myasthenia Gravis**

Potential to target more autoimmune diseases involving a **multi-antigen approach**

A **highly experienced team** in the field, with multiple publications

€10/20M series A

Aheads' Platform targets autoimmune diseases

More than 100 Immune diseases don't have curative treatments

Brain	Thyroid	Blood	GI Tract	Nerves	Skin	Bones	Muscles	Lung

Immune-diseases are ***chronic*** and ***degenerative*** diseases.

Some ***palliative*** treatments are available, producing ***strong secondary effects*** and not achieving the healing of the patient.

Ahead's platform has the potential to generate ***curative treatments.***

Thanks to a biomimetic MoA, ***secondary effects will be avoided.***

Ahead's core technology is ***leverageable across all diseases***, at ***affordable*** development and treatment costs.

Our solution is to REPROGRAM the Immune System, "repairing the mistake", at an affordable cost.
We "solve the problem", we don't mitigate it.

Ahead's Technology Platform is based on Bio-Mimicry

Bio-mimicry benefit is to avoid secondary effects and to activate both T and B-cell pathways

Normal immunity

Dendritic Cells (DCs)

Apoptotic Cells

Ahead **PRODUCT** is a PS-Liposome containing auto-antigens.

These PS-Liposomes can induce *antigen specific immune tolerance* through a *biomimetic process*, stopping the autoimmune attack against self-tissues, but keeping systemic immunity active.

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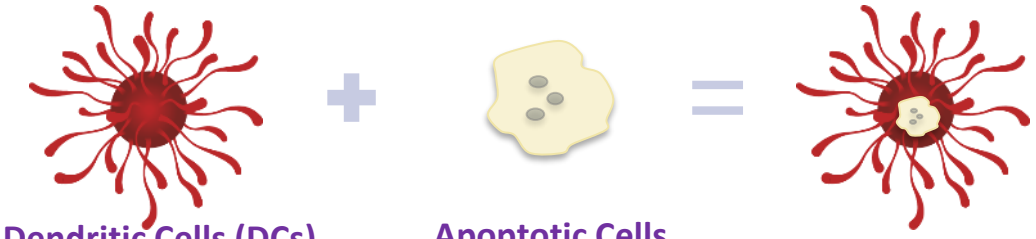

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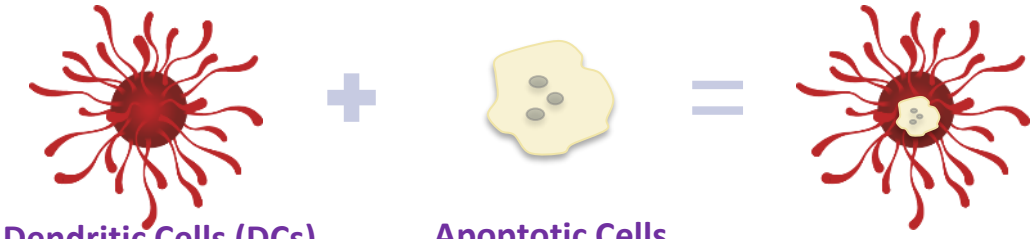

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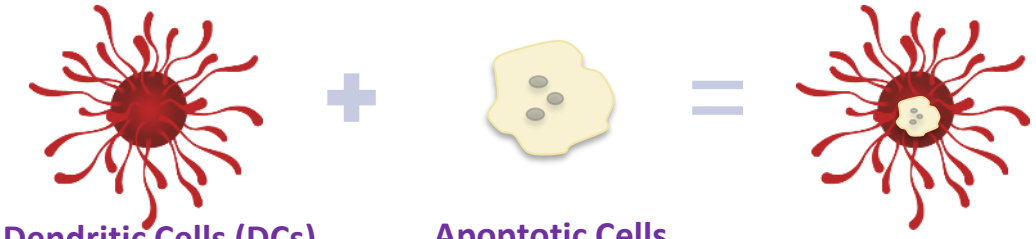

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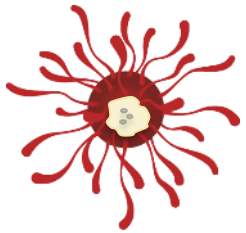
Dendritic Cells (DCs) +  Apoptotic Cells = 

Production of a tolerance signal

Platform **BIOMIMETIC**

Dendritic Cells (DCs) +  PS-Liposome = 

Tolerogenic DCs

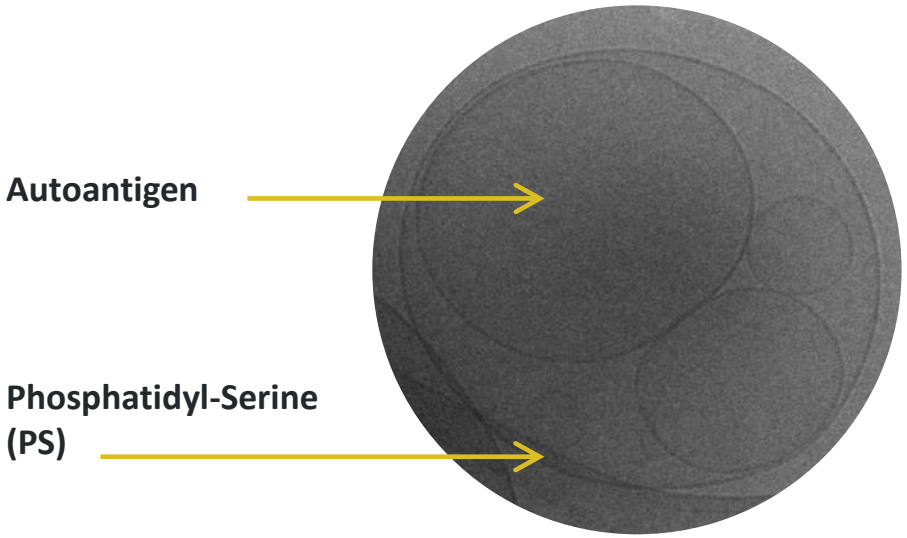
Antigen Specific tolerance signal

We STOP the Autoimmune Attack

Reprograming our immune system.

Ahead's Technology Platform addresses several diseases

PS-Liposome encapsulating Auto-Antigen(s): a versatile platform addressing many diseases



Multi-antigen encapsulation capability

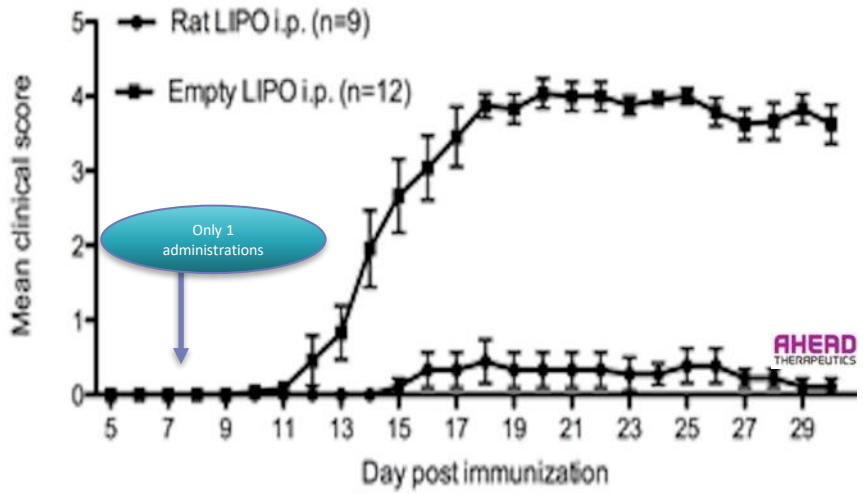
- Phosphatidylserine in the membrane identifies synthetic 'apoptotic cells', the signal for efferocytosis.
- Auto-antigens that trigger the autoimmune attack, are loaded into the liposomes to generate immuno-tolerance.
- Each disease has its own specific antigens.
- Liposomes are easy and cost effective to synthesize.

Ready for Efferocytosis & Antigen Specific Tolerance Generation

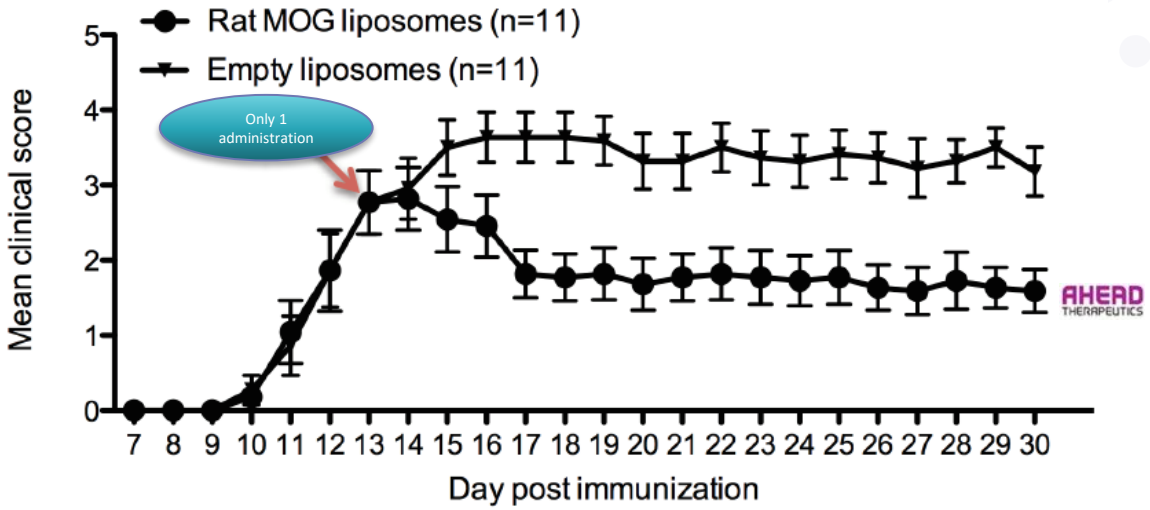
Rodriguez-Fernandez S,Master Thesis 2015

Ahead has a solid Technology Platform

PREVENTIVE Approach



THERAPEUTIC Approach



- *Multiple sclerosis was induced by the injection of MOG peptide. The 100% of the untreated mice display score 4 (full paralysis).*
- *When treated with Ahead's PS-liposome containing the Antigen MOG, clinical score of treated mice is between grade 0 and 1 (from non-symptoms to paralysis of the tail).*

Ahead's Key Team

A Highly professional, experienced and balanced Team

Marti Dalmases, MD, PhD, MBA
Chief Executive Officer

Marta Vives Pi, PhD
Chief Scientific Officer

Raul Insa, MD, PhD, MBA
Business Advisor

Bruna Barneda, PhD, MBA
Pre & Clinical Dev. Director

Silvia Rodriguez
CMC Director

Bernabé Zea, MSc
Business Advisor - IP strategy

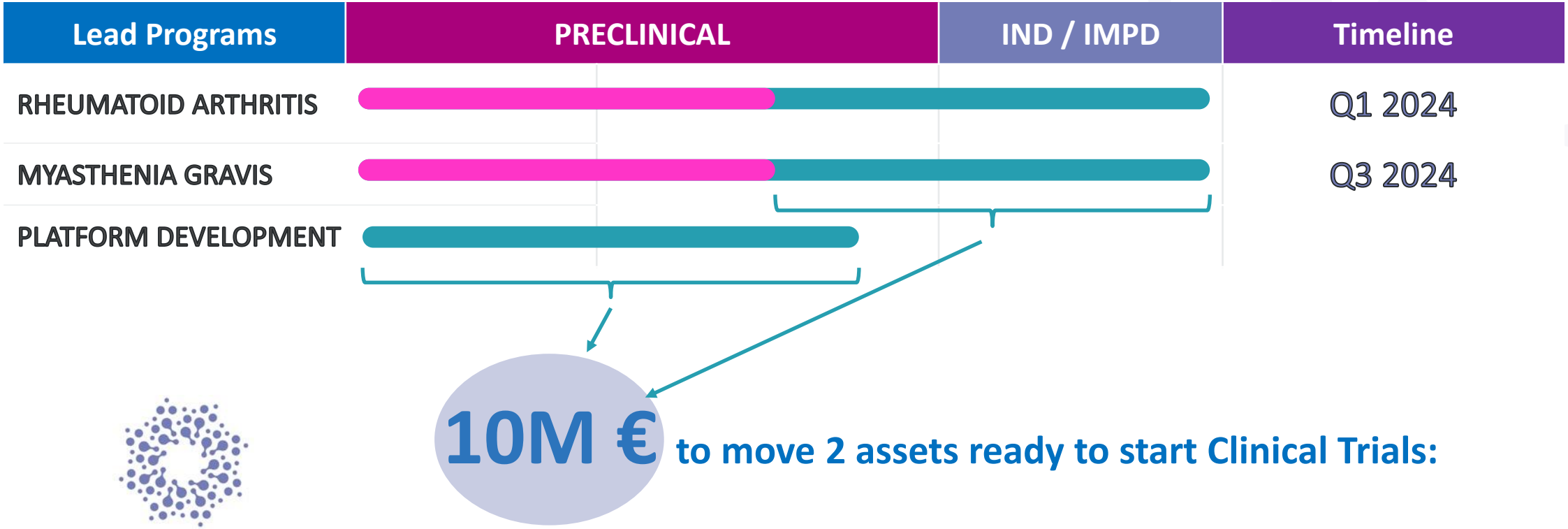
Daniel Maspoch, PhD
Liposome Technology Director

10M € to push 2 assets to IND/ 20M € adding Phase IIa for RA

	DISCOVERY	CANDIDATE	PRECLINICAL	PHASE I	PHASE II	PARTNER	OWNERSHIP
Lead Programs							
RHEUMATOID ARTHRITIS				Universitätsklinikum Erlangen	Vall d'Hebron VHIR	AHEAD THERAPEUTICS	100%
MYASTHENIA GRAVIS				HOSPITAL DE LA SANTA CREU I SANT PAU	UPMC	AHEAD THERAPEUTICS	100%
Secondary Programs in discussion for pharma partnerships							
MULTIPLE SCLEROSIS				with Cemcat		AHEAD THERAPEUTICS	100%
TYPE 1 DIABETES				with IGTP	IRB Lleida	AHEAD THERAPEUTICS	100%
MYOSITIS				with Vall d'Hebron VHIR	IGTP	AHEAD THERAPEUTICS	100%
CELIAC DISEASE				with La Fe		AHEAD THERAPEUTICS	100%
NEUROMYELITIS OPTICA				with HARVARD MEDICAL SCHOOL	CLÍNIC BARCELONA Hospital Universitari	AHEAD THERAPEUTICS	100%

Pipeline 2022 Pipeline YE-2026

The investment needed to reach the next **Key Inflection Point**



10M € **to move 2 assets ready to start Clinical Trials:**

- Antigen and Liposome GMP-like batch manufacturing.
- Safety Toxicology Package.
- Authorization for Human Clinical Trials (IND & IMPD).

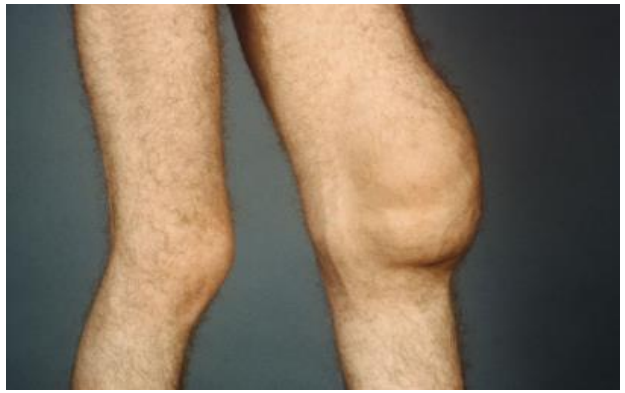
Lead Programs

Stunning Efficacy Results

Ahead shows efficiency in Rheumatoid Arthritis (1/4)

Disease

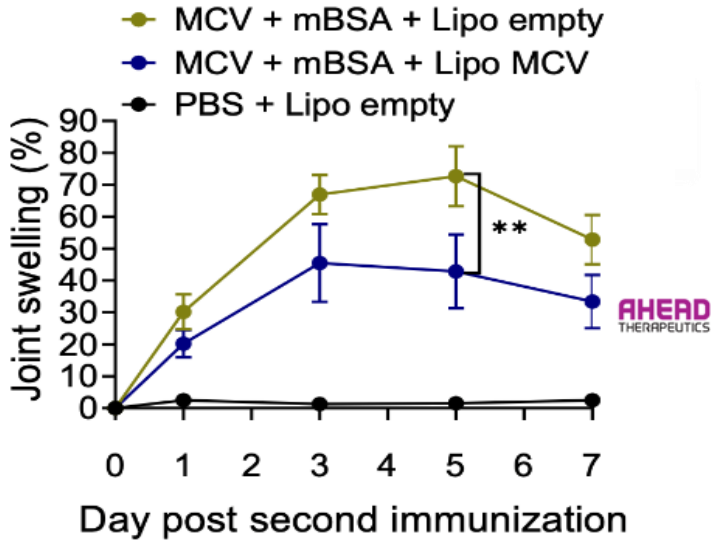
Out of every 100,000 people, 41 are diagnosed with RA every year. About 1.3M Americans have RA.

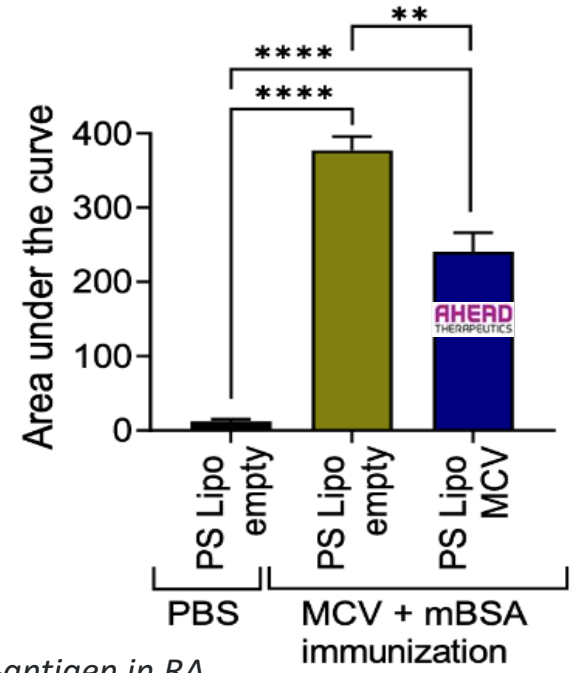


Joint's swelling is signing the disease

Results

Control of the Joint Swelling





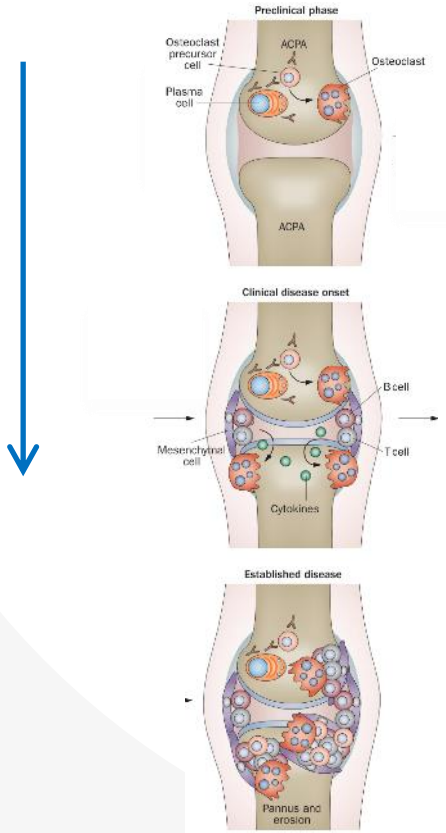
- *Mutated Citrulinated Vimentin (MCV) – Relevant auto-antigen in RA.*
- *Rheumatoid Arthritis was induced by the injection of MCV/mBSA in mice joints.*
- *When treated with Ahead's PS-liposome containing the Antigen MCV, the joints swelling decreases.*

Erlangen University. Georg Schett, 2020

Ahead shows efficiency in Rheumatoid Arthritis (3/4)

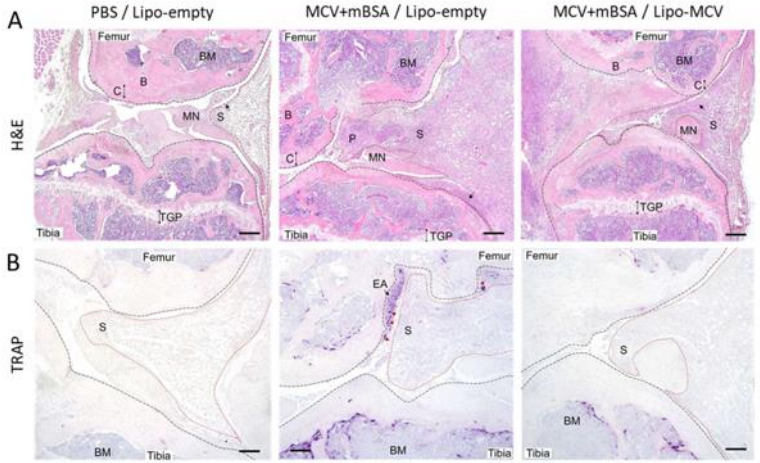
Disease

the over-activation of pre-osteoclasts degrades the bones of the joints



Results

PS-Liposomes dramatically reduce the eroded area and covers an *unmet medical need* in RA: the BONE DESTRUCTION.



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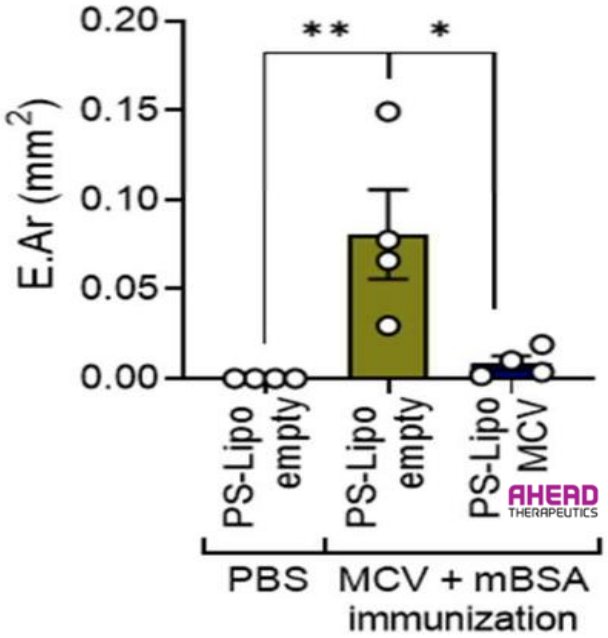

Ahead shows efficiency in Rheumatoid Arthritis (4/4)

Disease

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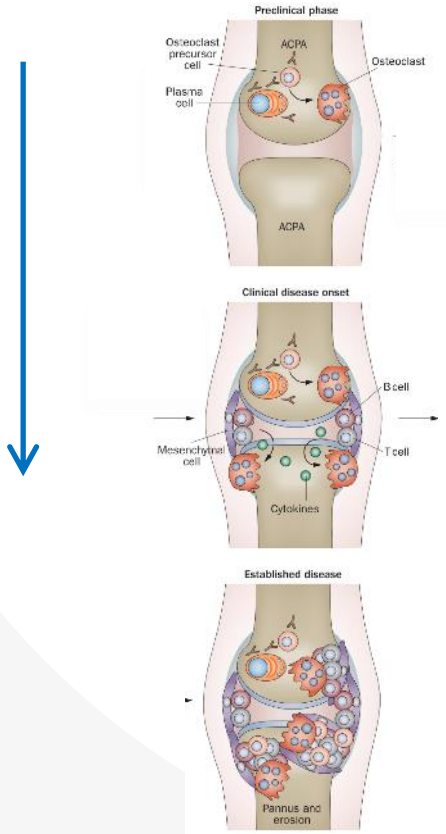
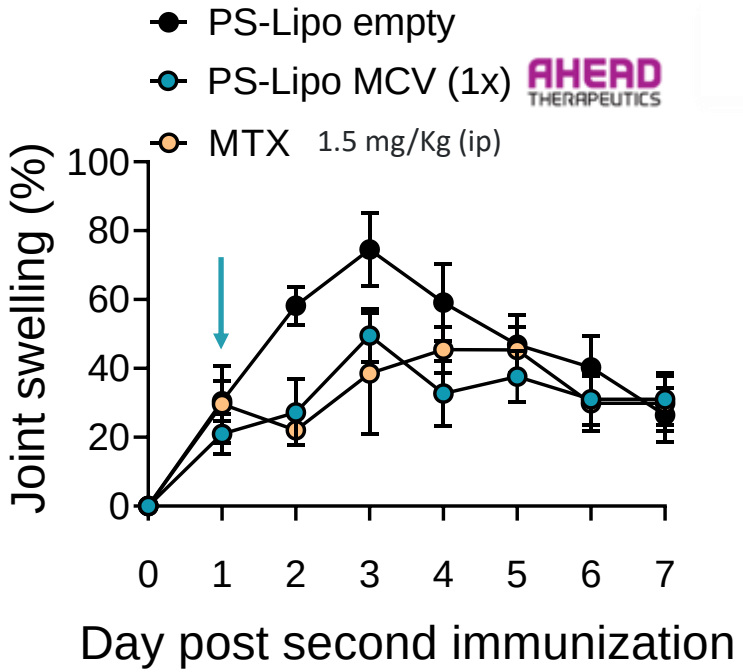
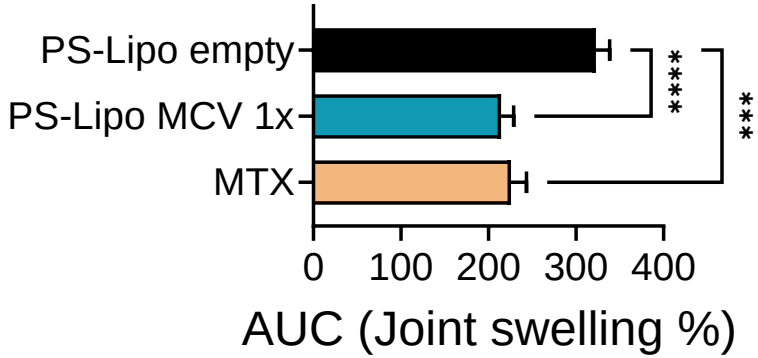


Results

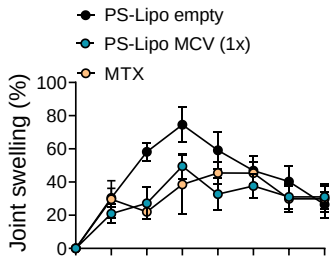
PS-Liposomes' obtain the same effect as the SoC Methotrexate, but having multiple advantages

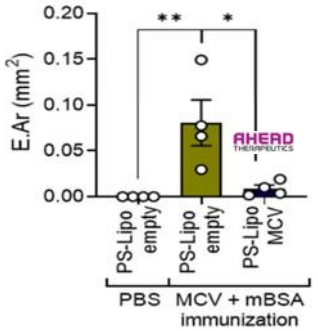


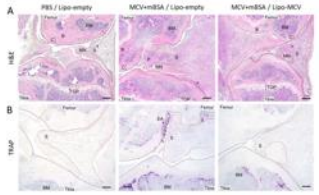


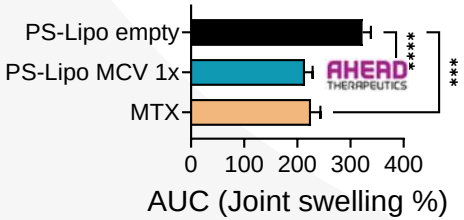
Erlangen University. Georg Schett, 2022

RA: Added value and advantages compared to SoC (MTX)









PS-Liposomes' value is clearly superior compared to Methotrexate SoC:

Beyond controlling the inflammation, Ahead's Therapy has three crucial COMPETITIVE ADVANTAGES that make the difference:

1. **Antigen Specific,** BUT non-systemic immune suppression, avoiding MTX side effects.

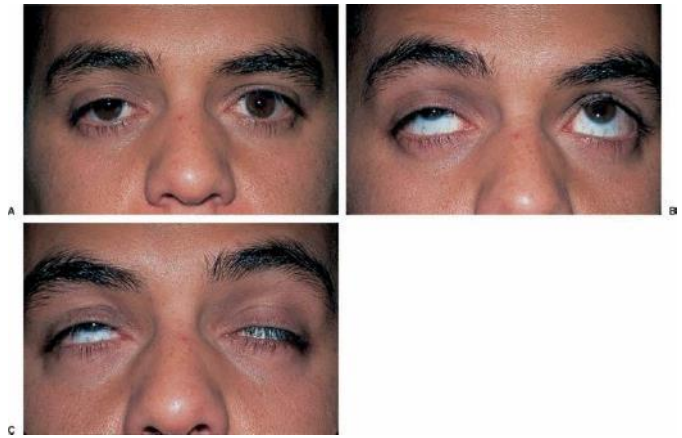
2. **Non-chronic treatment** like other ASIT therapy approaches and RA SoC, BUT PS-Liposomes generate tolerance during the first month.

3. To address a crucial **unmet medical need** in RA: bone destruction, whereas Methotrexate does not.

Ahead shows efficiency in Myasthenia Gravis (1/2)

Disease

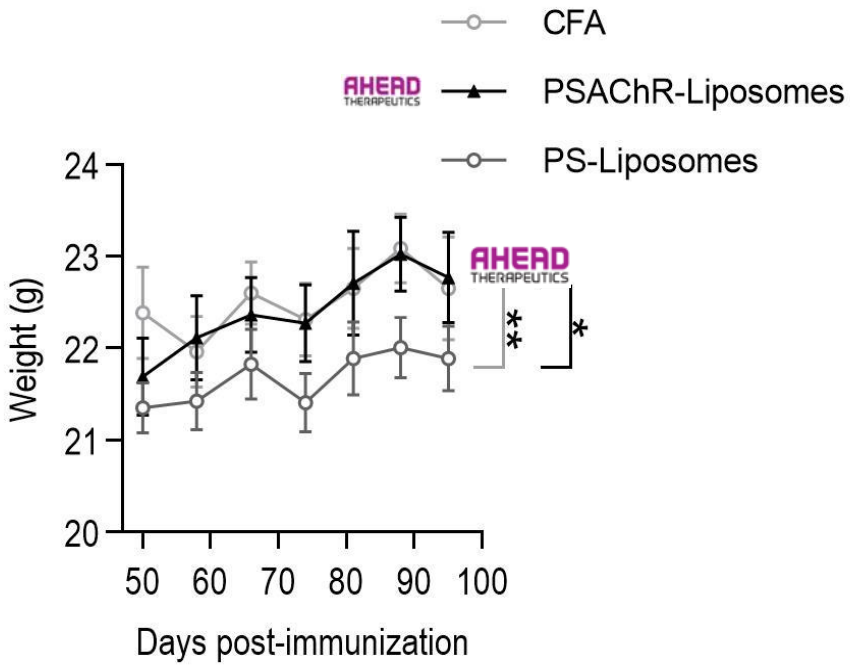
MG is a dishabilitating autoimmune disease involving muscular degeneration classified as a rare disease.



Institute of Myology (Paris). Dr. Le Panse, 2020

Results

PS-Liposomes' Improve Clinical Symptoms & Weight evolution is the same as Control Group



- *85% of MG patients has auto-antibodies against the receptor of Acetylcholine (AChR).*
- *MG was induced by the injection of AChR +CFA. Day 30, a boost-immunization (AChR +CFA) is performed; treatment starts at day 35 (**Therapeutic approach**).*

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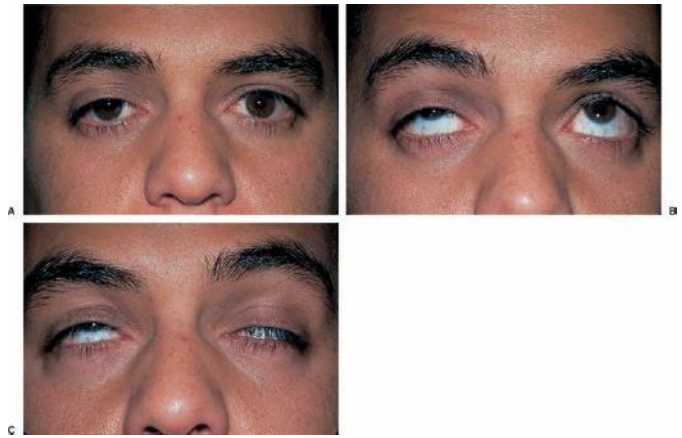

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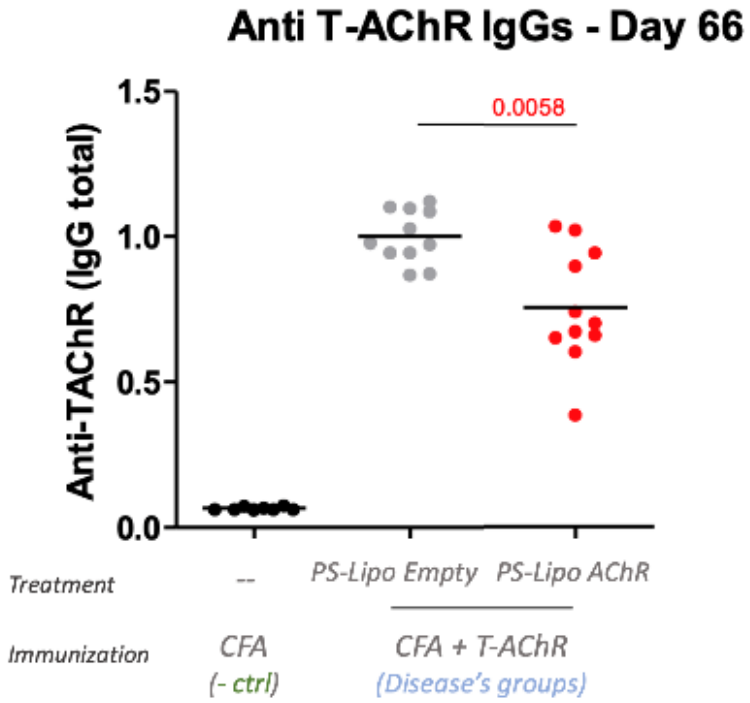
Results

PS-Liposomes' DECREASE AchR Antibodies, which are the primary drivers of the disease.



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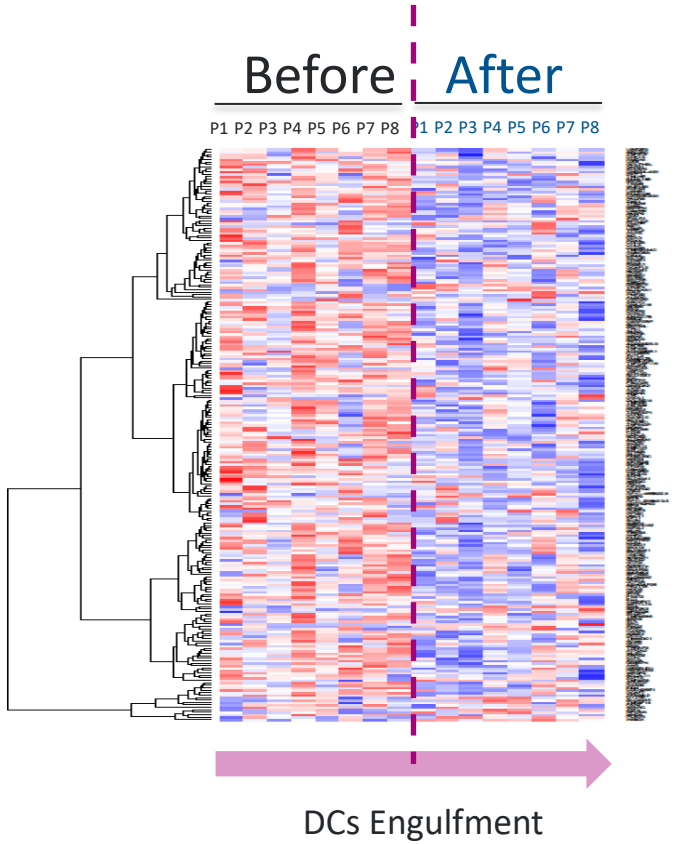
Ahead's MoA is transferable to human

Treatment with PS-Liposomes induce a tolerogenic profile in human Dendritic Cells

Results

- Tolerogenic phenotype induced by PS-Liposomes was characterized.
- Impairment of Dendritic Cells mediated autologous T-cells proliferation also in humans.
- Tolerogenic cytokine profile was also characterized and resembles the previous observed in mice.
- Transcriptomic profile after the engulfment of PS-Liposomes by Dendritic Cells shows a clear induction of genes involved in tolerance induction.

Gene transcription profile of dendritic cells coming from patients (P1-8) before and after the exposure to Ahead's PS-Liposomes



- Red: genes over-expressed
- Blue: genes under-expressed

Rodriguez-Fernandez S, Front Immunol, 2018 and Front Immunol 2019

Patent
&
Competitive Advantages

Ahead’s IP protection

Ahead's technology is widely protected through patent family WO2015107140.

The protection requested was broad and protects the tech platform.

FTO analysis was performed with ZBM Patents, with positive result.

The international patent application was filed on 01/16/15. At the moment, there is protection in Canada, United States, Mexico, Brazil, Europe, China, India, and Australia.

The European patent was granted on 03/14/2018
The Japanese patent was granted on 21/05/2019
The Australian, Mexican and Chinese applications have been intended to grant

AHEAD THERAPEUTICS

PRODUCT PATENT

Claim 1:
“A liposome encapsulating an autoantigen, wherein (i) the liposomes has a size comprised from 500 to 15000 nm; and (ii) the liposome membrane comprises phosphatydilserine (PS) in an amount comprised from 10 to 40% by weight with respect to the total membrane liposomal composition.”

Ahead's Competitive Advantages

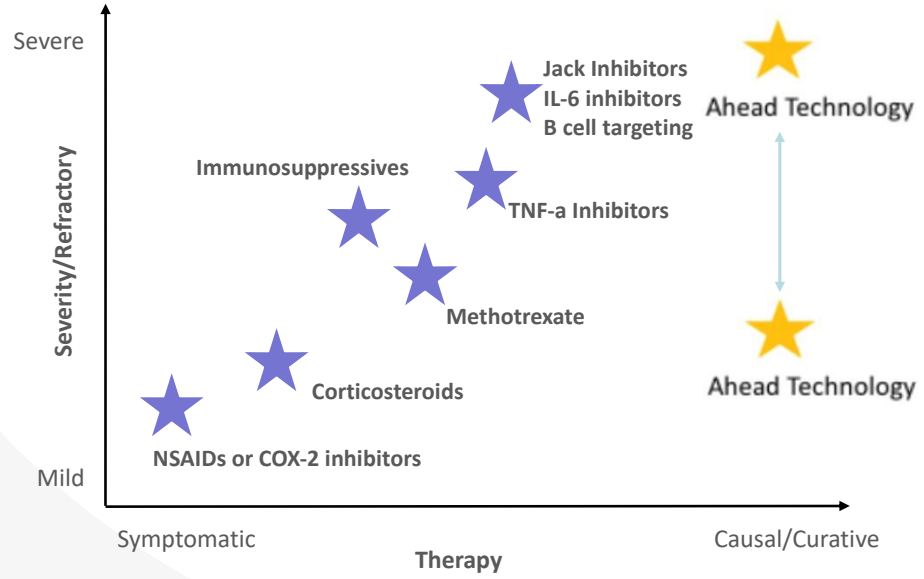
Biomimicry

Antigen Specific Immune Suppression

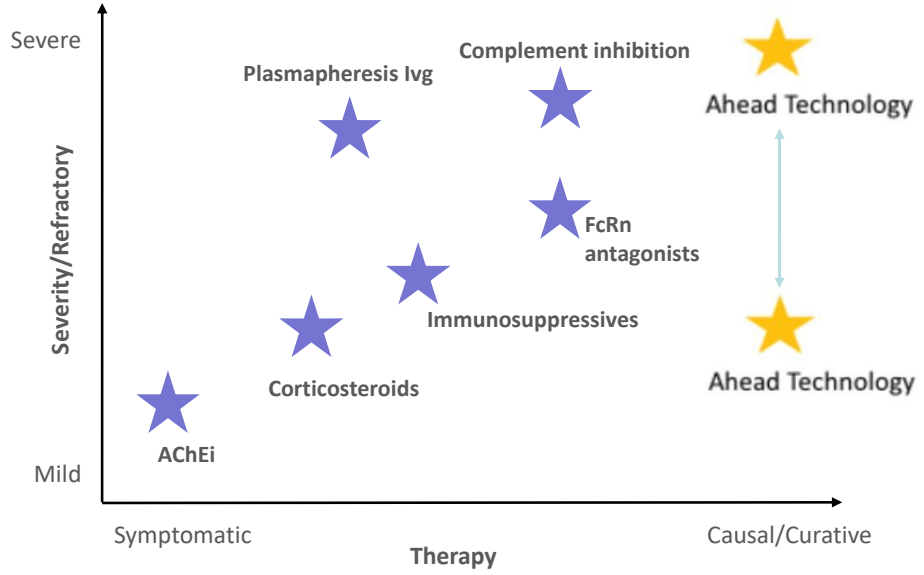
Unique Regime for Human Translation

Tech-Platform Potential

Rheumatoid Arthritis: Potential positioning for Ahead Therapeutics



Myasthenia Gravis: Potential positioning for Ahead Therapeutics



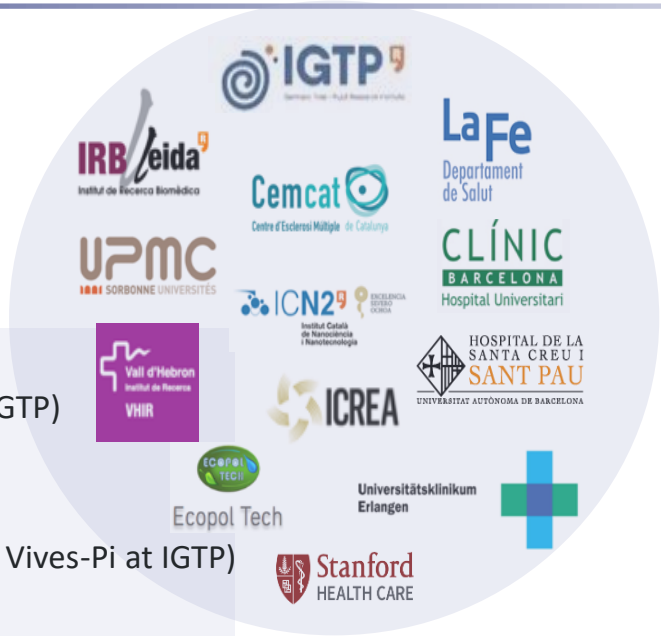
Ahead's ressources & Strategic Alliances

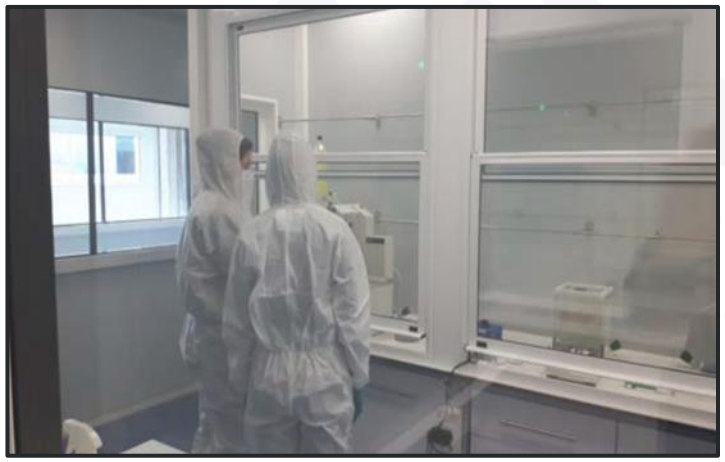
Immunology unit (IGTP) – Dr Marta Vives Pi (CSO)

- **T1D studies**
- MoA and platform development (BIO assays)

Proof of Concept (PoC):

- **Rheumatoid Arthritis:**
  - ex-vivo assay (Dr. Sara Marsal Vall d'Hebron and Dra. Vives-Pi at IGTP)
  - in vivo assay (Pr. Georg Schett – Erlangen University)
- **Myasthenia Gravis:**
  - ex-vivo assay (Dra. Elena Cortes and Dr. Eduard Gallardo and Dra. Vives-Pi at IGTP)
  - in vivo assay (Dra. Rozen La Panse – Institute of Mycology Paris)
- **Multiple sclerosis:**
  - ex-vivo and in vivo assays Dr. Carmen Espejo and Dr. Xavier MontalbanCEMCAT
- **Celiac Disease:**
  - ex-vivo assay (Dra. Carmen Ribes-Konick Hospital de la Fe de Valencia)
- **Neuromyelitis Optica:**
  - ex-vivo assay (Dr. Albert Saiz – Hospital Clínic Barcelona and Dra. Vives-Pi at IGTP)
  - In vivo assay (Dr. Michael Levy – Massachusetts Hospital)
- **Histidyl-t-RNA synthetase syndrome:**
  - ex-vivo assay (Dr. Mark Genovese - Standford)
  - in vivo assay (Dr. Albert Selva - Vall d'Hebron hospital and Carmen Espejo - CEMCAT)





Clean room facility

- Liposomes' scalability / lyophilization
- Liposomes' manufacturing

Strategic alliance with the Analytics chemistry department University of Barcelona

- Liposomes' characterization
- Development of Analytical methods

Investment case

10M € / 20M €

To *Bring both leading assets to IND / IMPD*

To *perform first Human PoC with RA asset*

Ahead is raising 10M - 20M € series A to push MG to IND and RA to Phase IIA

Use of Proceeds

Resources needed x milestones

X	Key Milestones (Inflection Points)	Year 1				Year 2				Year 3				Year 4			
Rheumatoid Arthritis (RA) asset		T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4
1	GMP-like batch RA PS Liposome completed	2.662.656		X													
2	Toxicology ended / IND enabling phase			2.027.525		X											
3	Human PoC Clinical Trial IIab succeed (80 patients)								8.125.539						X		
	Total asset develp. timeline & costs	12.815.721													X		

		Year 1				Year 2				Year 3				Year 4			
Myasthenia Gravis (MG) asset		T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4
4	GMP-like batch MG PS Liposome completed	1.891.908				X											
5	Toxicology ended / IND enabling phase			2.344.855						X							
	Total asset develp. timeline & costs	4.236.763								X							

		Year 1				Year 2				Year 3				Year 4			
Tech-platform continuous development		T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4	T1	T2	T3	T4
6	Tot costs for continous Platf. Develop.	3.158.958															X

TOTAL Business Case Costs	20.211.441				X

	Year 1	Year 2	Year 3	Year 4
Total funds needed x year	5.155.312	4.502.834	5.541.017	5.012.277
Cummulated funds needed	**5.155.312**	**9.658.146**	**15.199.164**	**20.211.441**

Existing deals in the field

A disclosed deal for $800M, for an asset in early stage of development

COMPANIES	ACQUIRERS	DEAL DETAILS
Parvus Therapeutics	Novartis / Genentech (A Member of the Roche Group)	Single asset licensing deal, T1D, **$800M**
Topas Therapeutics	Boehringer Ingelheim	Undisclosed
COUR	Takeda	Single asset licensing deal, celiac disease, undisclosed
ANTOLRX	Pfizer	Single asset licensing deal, T1D, undisclosed

Ahead's potential acquirers

Status: periodic updates/MTA/co-development programs agreements

Company	RA	MG	T1D	MS	CEL	NMO	OTH
Novartis	*		*		*		
Grifols		*				*	
Roche/Genentech	*			*	*		*
Amgen	*		*		*		
Eli Lilly	*		*		*		
J & J	*		*		*		
Pfizer	*		*				
MERK	*						
JT Pharma			*	*			
Asahi Kasei Pharma	*		*	*	*		
ARGEN-X		*				*	
SANOFI			*	*	*		
TAKEDA		*				*	
Mitsubishi Tanabe	*			*			*

TD1 (type 1 diabetes); MS (multiple sclerosis); CEL (Celliac Disease); NMO (Neuromyelitis Optica); MG (Myastenia Gravis); RA (Reumathoid Arthritis); OTH (Other AD)

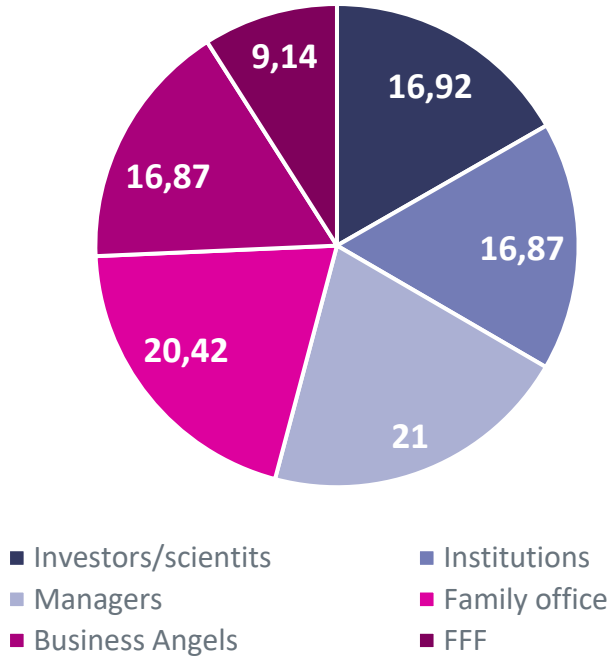
Business Model - Strategy

- First Assets Dev.; financed by leading Investor (+ followers):
  - 1st Key-Value Inflection Point for the two assets: until IND: 10 M €.
  - Full Program: + First Clinical Trial Phase IIa for first asset: 20 M €.

- Collaborations for co-development / sub-license; candidates:
  - Large Market Indications: TD1 / MS / Rheumatoid Arthritis / Cel. Disease
  - Orphan Drug / Rare Diseases: MG / NMO / A-Synt. Syndr. (MYO).

Cap Table and Previous Investments

Cap Table



Previous investments

Type of funds	Amounts
Private Capital	4.213 M €
Grants from Government & UE	2.142 K €
Debt (loans without guaranties)	325 K €
TOTAL =	**6.680 M €**

AHEAD THERAPEUTICS

HELP PEOPLE SUFFERING from autoimmune diseases,

offering them something BEYOND a palliative treatment,

that is, a potential treatment for

PREVENTION or HEALING