Programa Cooperación Farma-Biotech
Neurociencias

NT-KO-003

A new oral treatment for Multiple Sclerosis based on a novel mechanism of action

Neurotec Pharma

Barcelona, 15 de febrero 2011

CataloniaBIO
Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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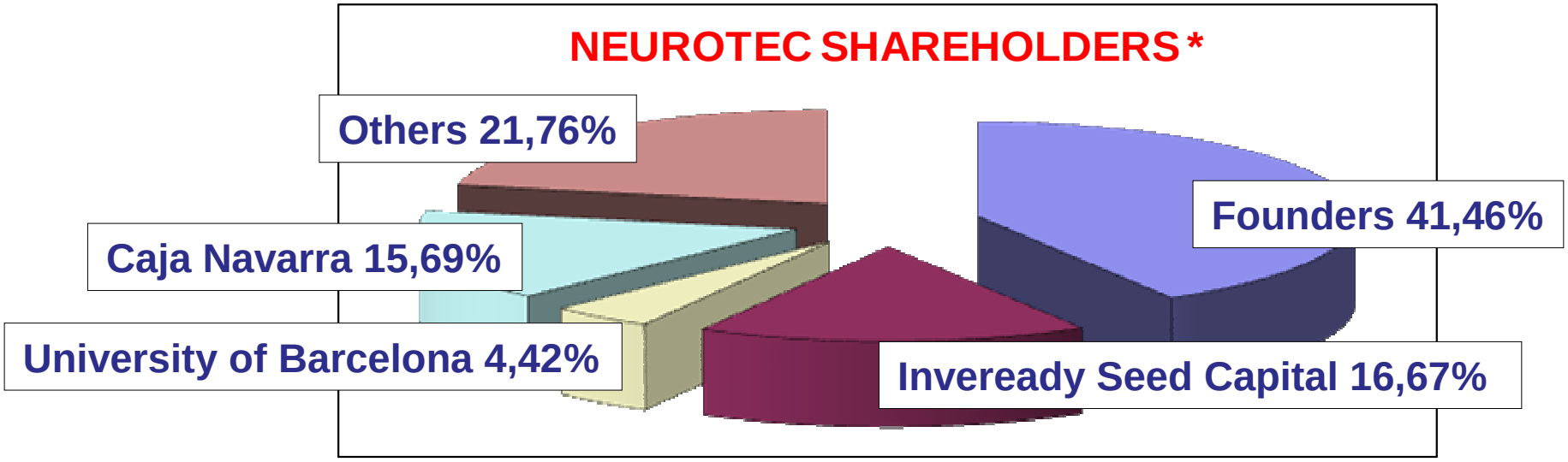
1. Who we are

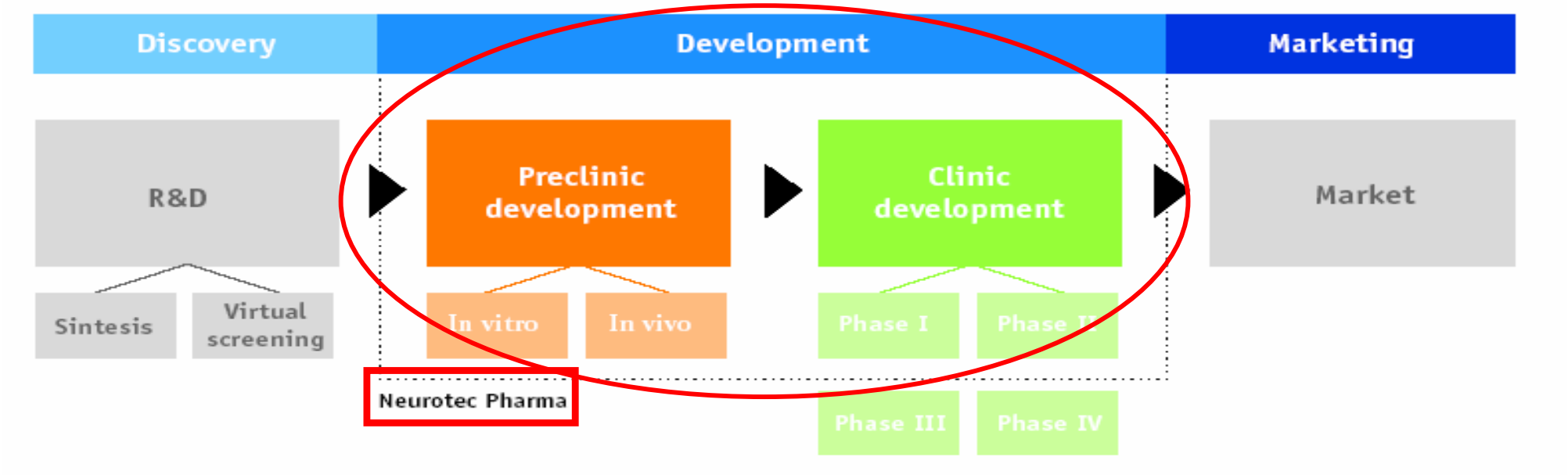
Neurotec Pharma S.L. is a spin-off of the University of Barcelona founded in 2006 and located in the Bioincubator PCB-Santander in the Barcelona Science Park, Spain.



** Current status after the capital increase (300K) made in December 2010*

1.What we do

Our business model is to develop **new treatments for CNS diseases** related with inflammation and neurodegeneration from **its Preclinical Phase up to Clinical Phase II** with the aim to **increase their values and transferring** them to third parties by either commercialization or out licensing.



1. Organization chart

MARCO PUGLIESE, PhD
CEO

Javier Bustos
Project Manager

Juan Espinosa, PhD
CSO

JM Echarri
CFO

Researcher
Noemí Virgili

Researcher
Pilar Mancera

Researcher
Andrea Pasten

MS and ALS animal models (EAE mice and mSOD1 transgenic mice)
Other animals models (Stroke, Neurodegeneration, Parkinson)
Primary and mixed microglial cell culture
Histology and Immunochemistry
Molecular biology

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1. Our partnership

ADVISORY BOARD

Dr. Pablo Villoslada, Neuroimmunology Group, IDIBPAS, Barcelona.

Dr. Xavier Montalban, Hospital Vall d'Hebron, Barcelona.

Dr. Alex Rovira, IDI, Hospital Vall d'Hebron, Barcelona.

Dr. Rafael Arroyo, Hospital Clínico San Carlos, Madrid.

Dr. Ralph Gold, St. Josef-Hospital/Ruhr-University Bochum

Dra. Nicole Mahy, Neurochemistry Group, UB-IDIBAPS, Barcelona

Dr. Manuel Rodríguez, Neurochemistry Group, UB-IDIBAPS, Barcelona

Dr. Eduardo Cunchillos
Innoqua, Barcelona

IDIBAPS
Institut D'Investigacions Biomèdiques August Pi i Sunyer

INVEREADY

Vall d'Hebron Hospital

cajanavarra

Hospital Clínico San Carlos

JANUS DEVELOPMENTS
Bridging the gap

Ruhr-Universität Bochum

IDIFARMA
INVESTIGACIÓN, DESARROLLO E INNOVACIÓN FARMACÉUTICA

UNIVERSITAT DE BARCELONA

salutis RESEARCH

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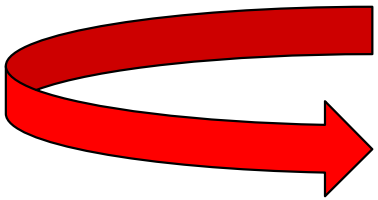
2.a Objectives 2011-2013

Development of a **new oral treatment** for **MS** and **ALS** based on **reprofiling of the drug (NT-KO-003)** with **a novel mechanism of action.**

STRATEGIC OBJECTIVES:

- **Successful completion of a clinical phase (IIa) in patients with MS.**
- **Successful completion ALS preclinical studies: CTA/Orphan drug application.**



ADVANCELL
advanced in vitro cell technologies, s.l.

Co-development agreement December 2010

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2.b Therapeutic focus: MS

√ MS is a **common neurological disease of unknown aetiology** affecting more than 2 million people worldwide, including 30-40,000 in Spain.

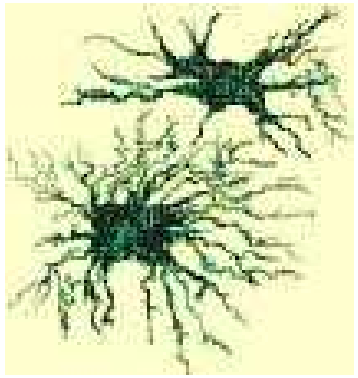
√ MS is **primarily an inflammatory disorder** of the brain and spinal cord in which focal lymphocytic infiltration leads to damage of myelin and axons that produces significant disability.

√ MS is the **commonest cause** of neurological disability in **young and middle-aged adults** and has a major physical, psychological, social and financial impact on patients and their families, friends and bodies responsible for health care.

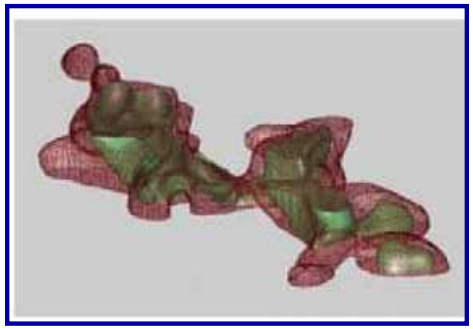
√ At present, one of the major challenges in the treatment of the disease is the **lack of effective strategies to slow disease progression.**

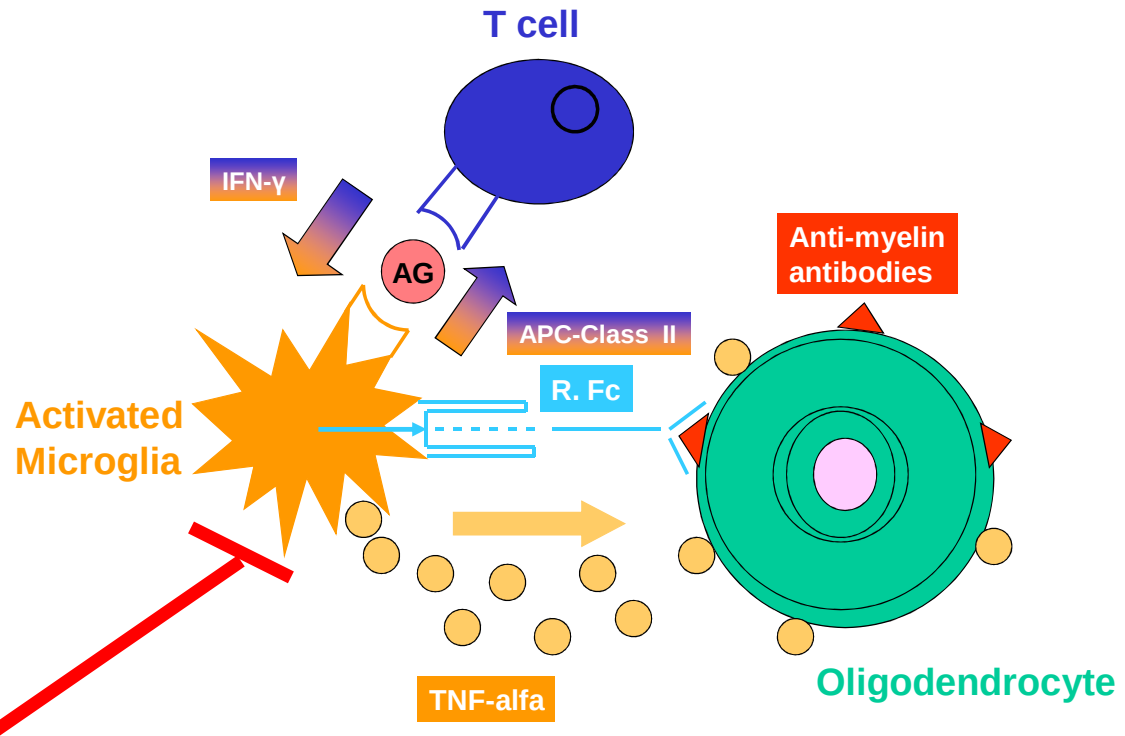
2.c Innovative mechanism of action

TARGET: Microglial cells



DISCOVERY:
Potassium Channels as pharmacological target on microglial cells





NT-KO-003

- Inhibition of glial activation
- Reduction of oxidative stress
- Decrease release of pro-inflammatory cytokines
- Neuroprotection (Direct and indirect effect)

2.d Differential features facing the market

√ **Authorized products** with **limited efficacy and significant side-effects** (Different forms of Interferon beta; Chemotherapeutic agents; Glatiramer acetate, a random polymer; Monoclonal antibodies).

√ **Other methods of treatment under research** in MS with **higher efficacy but significant** side-effects (Fingolimod (approved in USA), Cladribine, Fumaric acid; Monoclonal antibodies)

WHAT IS NECESSARY

1) Developing **more efficacious** drug products (targeting inflammation but also neurodegeneration) to slow or block disease progression.

2) **Safer** drug products (avoiding life-threatening adverse events (fatal infections, cancer) and non-serious adverse events that impairs quality of life (e.g. flu-like symptoms).

3) **Oral administration** and with good profile for an eventually **combination therapy.**

NEUROTEC PROPOSAL

NT-KO-003 AS SAFE, EFFICACIOUS AND EASILY ADMINISTERED TREATMENT FOR RR-MS

2.e Current status of development

Drug substance and manufacturing

• **NT-KO-003** is a **generic compound (small molecule)** used systemically (IV and oral) for more than 25 years for acute and chronic treatment of peripheral diseases.

• **NT-KO-003** has been used for a long time in patients and thus **well documented clinical experience** in humans exist to establish **its safety profile** with oral doses. Consistent preclinical and clinical safety package available.

√ **API with CEP available**: **Indukern S.A, Barcelona, Spain**

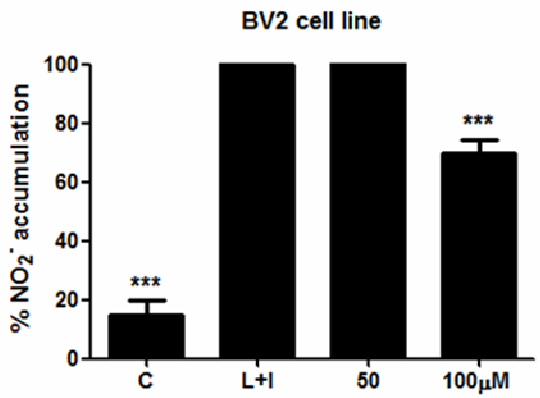
√ **Pharmaceutical development of the formulation and development of analytical methods.**

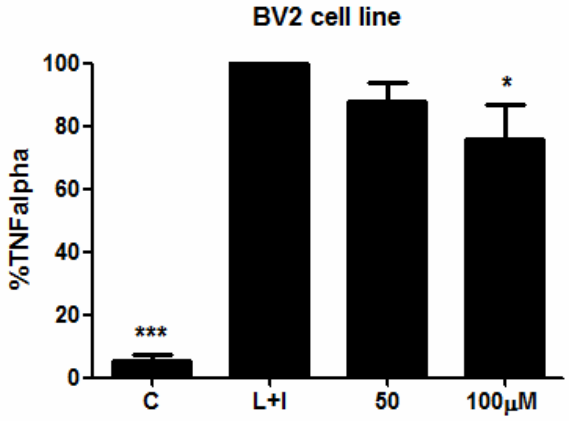
√ **GMP manufacturing of clinical batches and logistics management of medication for the trial.**

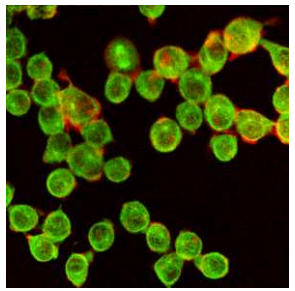
→ **Idifarma SA, Noáin, Navarra, Spain**

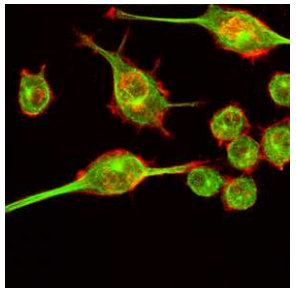
2.e Current status of development

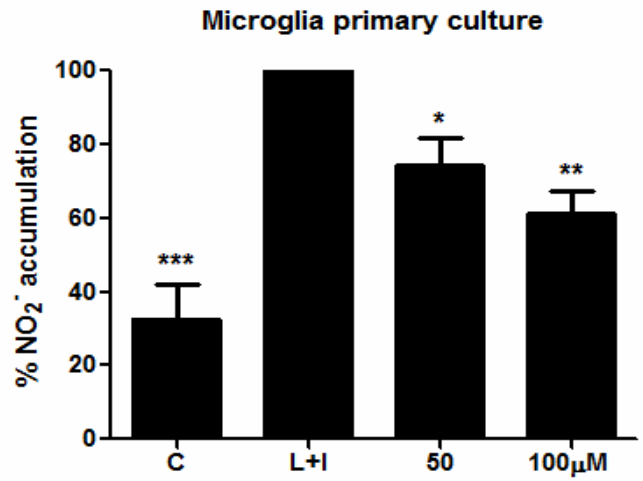
Preclinical *in vitro* studies

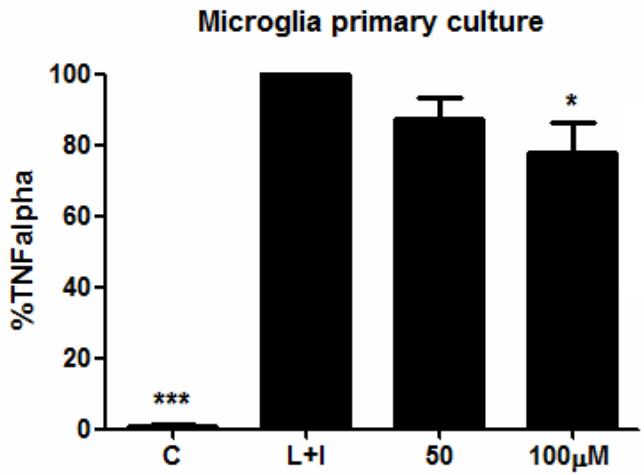








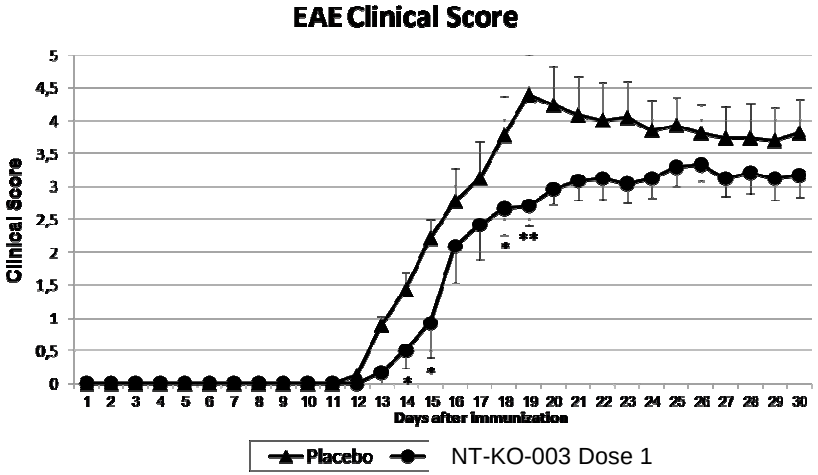


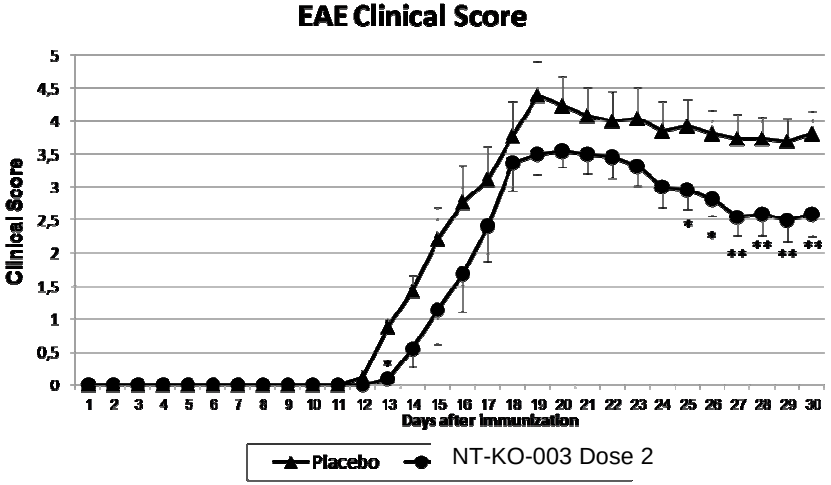


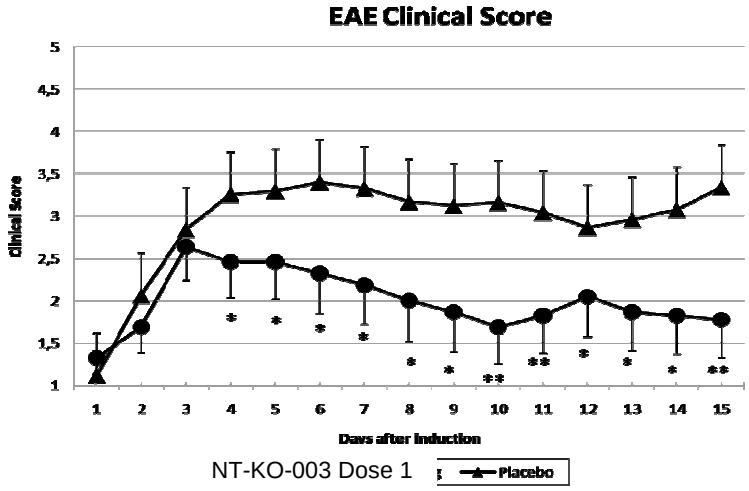
Anti-inflammatory effects of NT-KO-003 on microglial cell line and primary culture

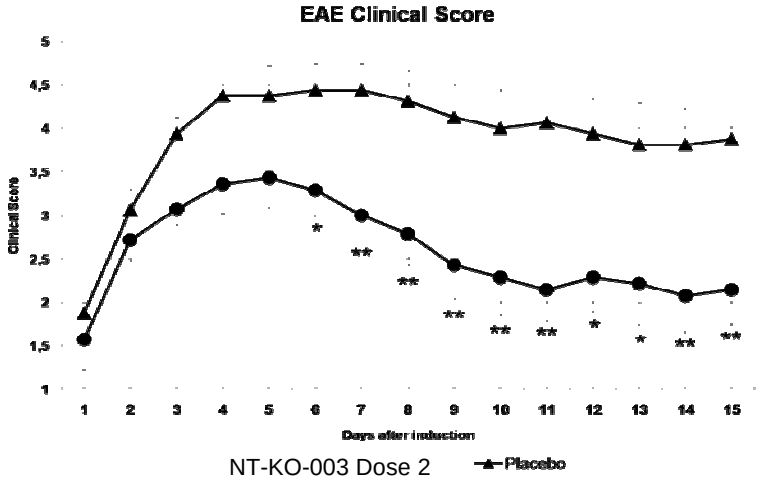
2.e Current status of development

Preclinical *in vivo* studies: Efficacy of NT-KO-003* on EAE C57BL/6J mice









**** Doses used are between 50 and 750 times lower than the current marketed drugs***

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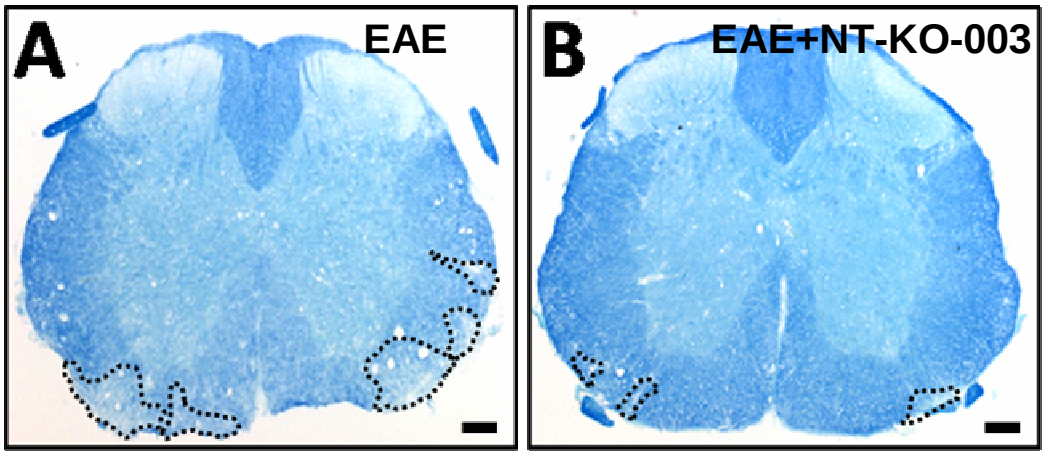
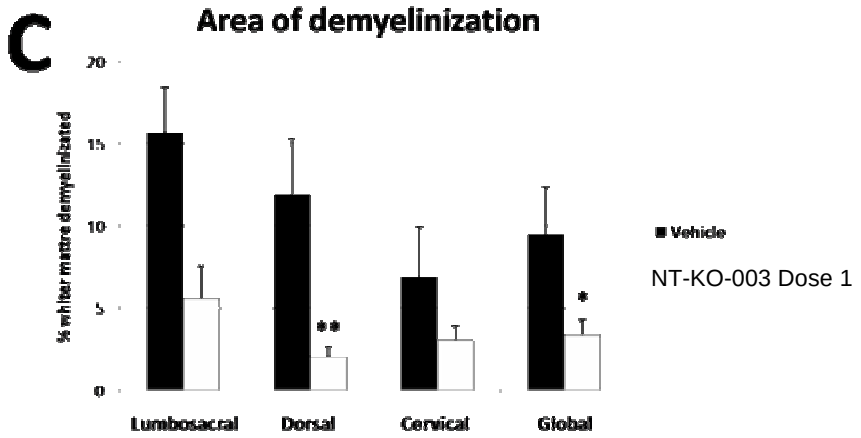
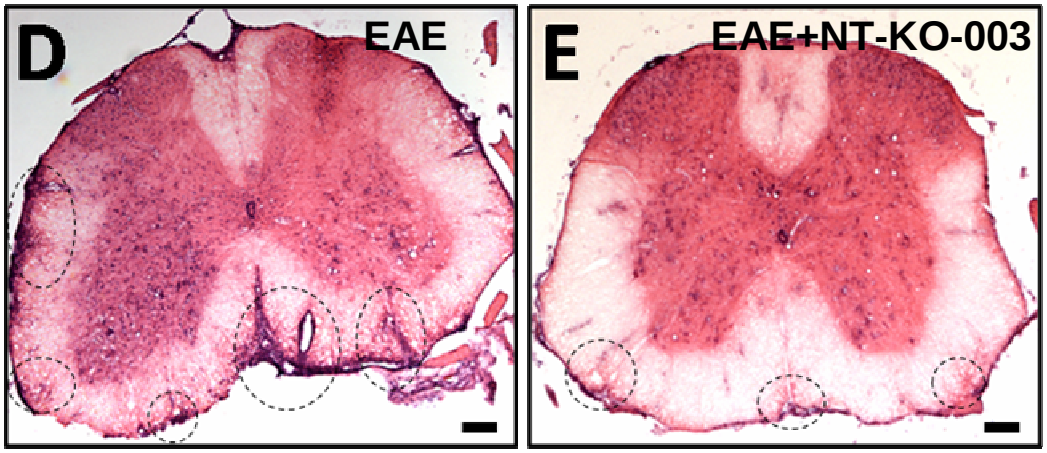
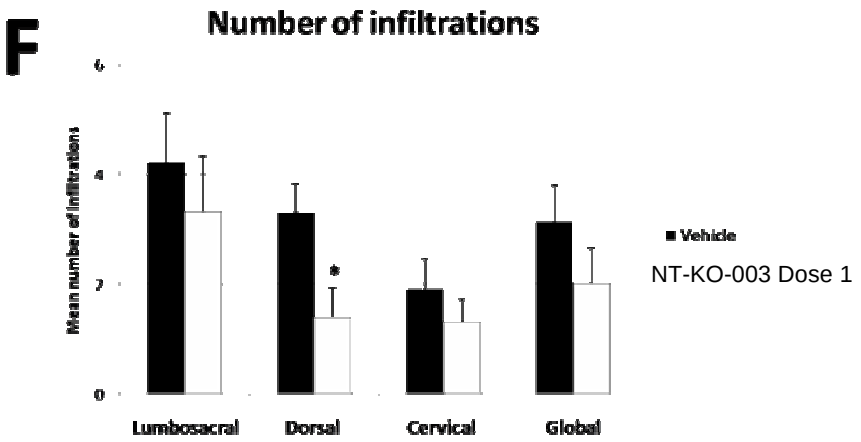
2.e Current status of development

Histological studies: NT-KO-003 reduces demyelinization and cell infiltration









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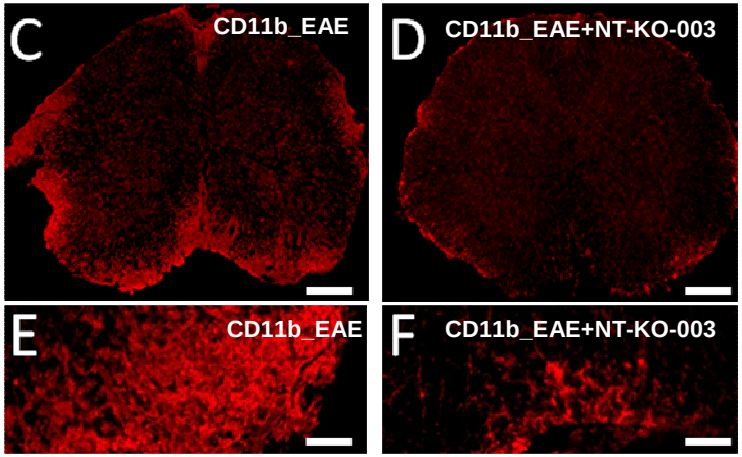
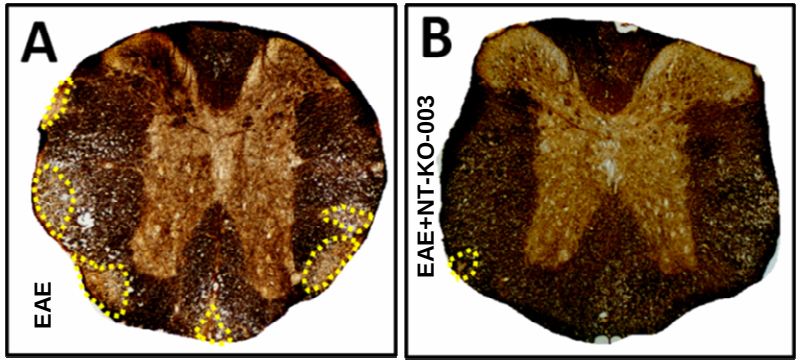
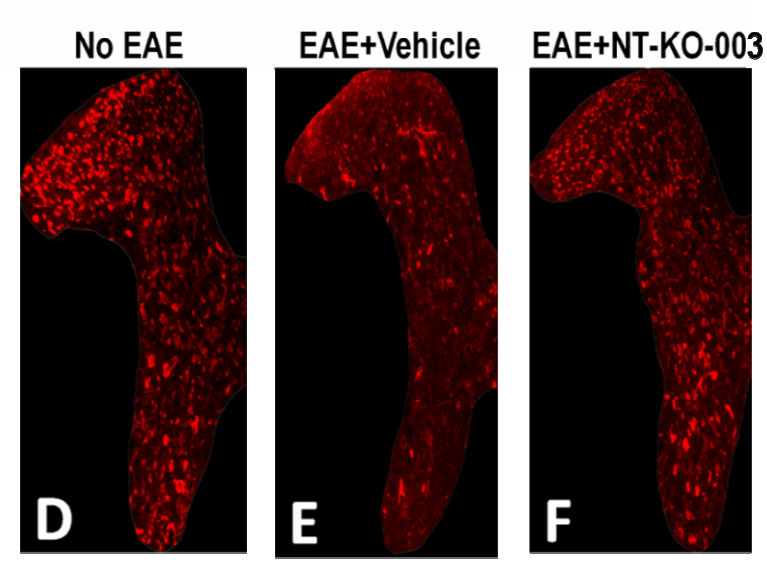
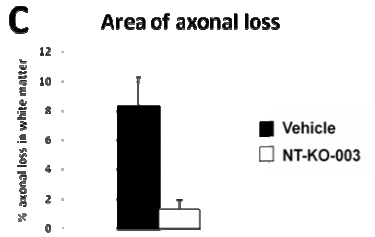
2.e Current status of development

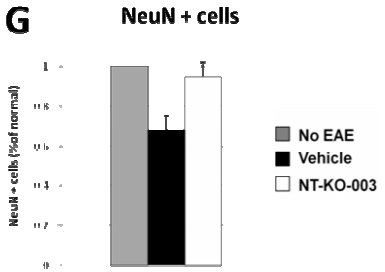
Histological studies:
NT-KO-003 decreases microglial reactivity and induces neuroprotection

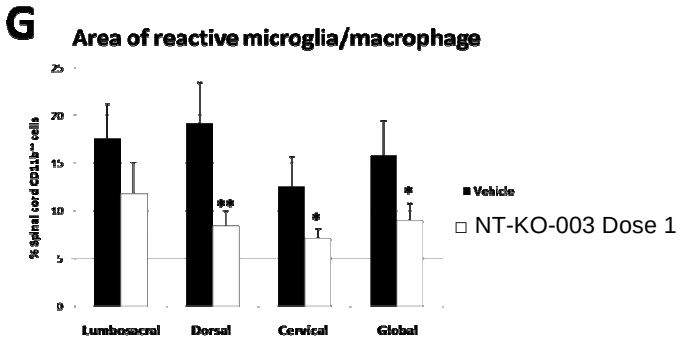












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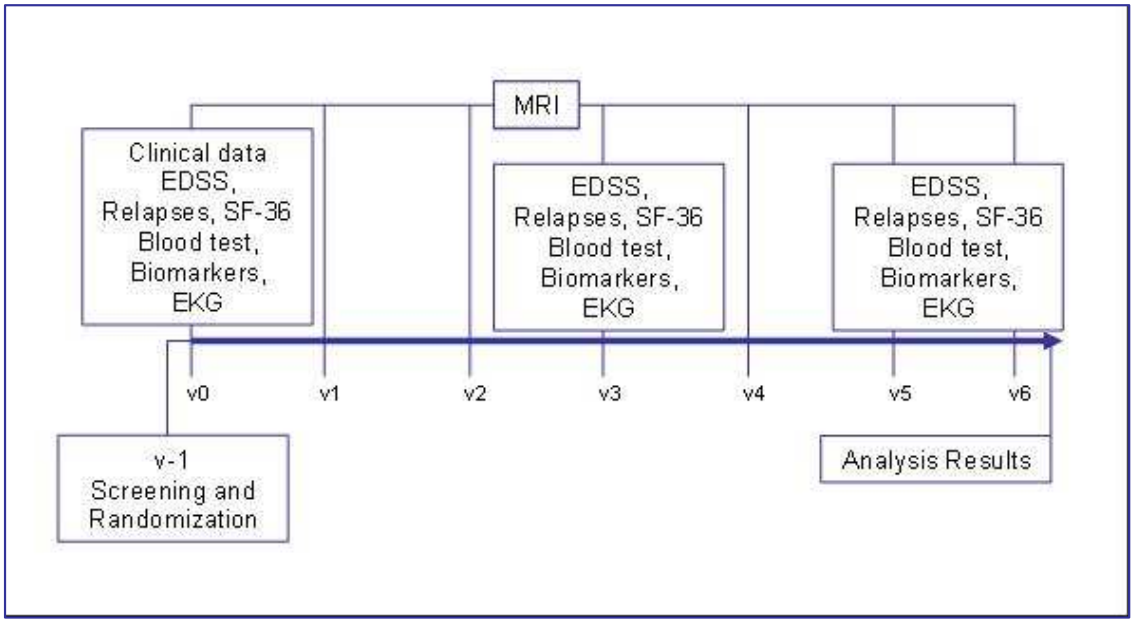
2.e Current status of development

REGULATORY

√ **June 2010: SCIENTIFIC ADVICE to Health Authority in Spain**

√ **January 2011: CTA to Ethical Committees of Hospitals and Health Authorities in Spain and Germany**

NT-KO-003 oral treatment for RR-MS.
Duration: 6 months.
Multicenter, Double Blind, Randomized, Placebo-controlled study.
Patients: 105 patients with RR-MS
Centers: 11 Spain hospitals + 3 German Hospitals
Start of subject enrolment: April 2011
End of subject enrolment: March 2012
End of study: December 2012
Report : First semester 2013



2.f Second application: ALS

ALS is a progressive, fatal, **neurodegenerative disease** caused by the degeneration of **motor neurons**, the nerve cells in the central nervous system that control voluntary muscle movement. The median survival is 3 to 4 years, and 50% of patients die within the first three years after onset of symptoms.

THERE IS NO CURE FOR ALS:

The FDA granted the orphan drug status for RILUTEK in 1995

NEUROTEC STUDIES: COMPLETED

***a) In vitro* NT-KO-003 efficacy in SOD1 transgenic mice cell culture (Anti-inflammatory effects)**

***b) In vivo* pilot study in ALS animal model (Delay Onset, increase survivor and motor responses)**

Pre-clinical regulatory dossier to perform CTA/Orphan drug application

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2.g IPR Protection

√ Patent protection in a specific environment

A) NT-KO-003 for use in the treatment of a CNS autoimmune demyelinating disease

√ **January 2010: European Patent application**
√ **January 2011: PCT Application**

√ **December 2010: Study of the freedom to operate for a NT-KO-003 - containing composition for use in the treatment of multiple sclerosis**

B) NT-KO-003 for use in the treatment of Amyotrophic Lateral Sclerosis

√ **August 2010: European Patent Application**

√ Differentiation of generic and off-label use per dose and formulation

The efficacy of NT-KO-003 is between 50 and 750 times lower than the current marketed drugs

2.h Pitfalls & Risks to be considered

RISK

- Risk related to intellectual property.
- Recruitment of patient.
- Limited or no detectable efficacy in patients.
- Off label use.

CONTINGENCE PLAN

- Generation of new data to support the efficacy and safety of doses protected.
- The proposed schedule is realistic. Contract milestones with the CRO.
- More information using other variables (eg. PET study).
- The concentration of effective doses of NT-KO-003 makes it impossible to carry out cross- prescription.

3. Availability for cooperation

1) Out Licensing EM and ALS projects

2) Collaboration to perform Phase IIa clinical trial in ALS

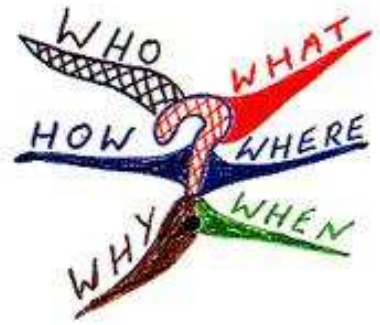
3) Collaboration to perform Phase IIb clinical trial in MS

4) Availability of our technology platform to test molecules for its use in CNS diseases

THANK YOU !!

GRACIAS !!

GRAZIE !!



QUESTIONS?