Programa Cooperación Farma-Biotech

X encuentro (27 de noviembre de 2013)

Oral NT-KO-003 for the Treatment of Multiple Sclerosis

Madrid, 27 de noviembre de 2013

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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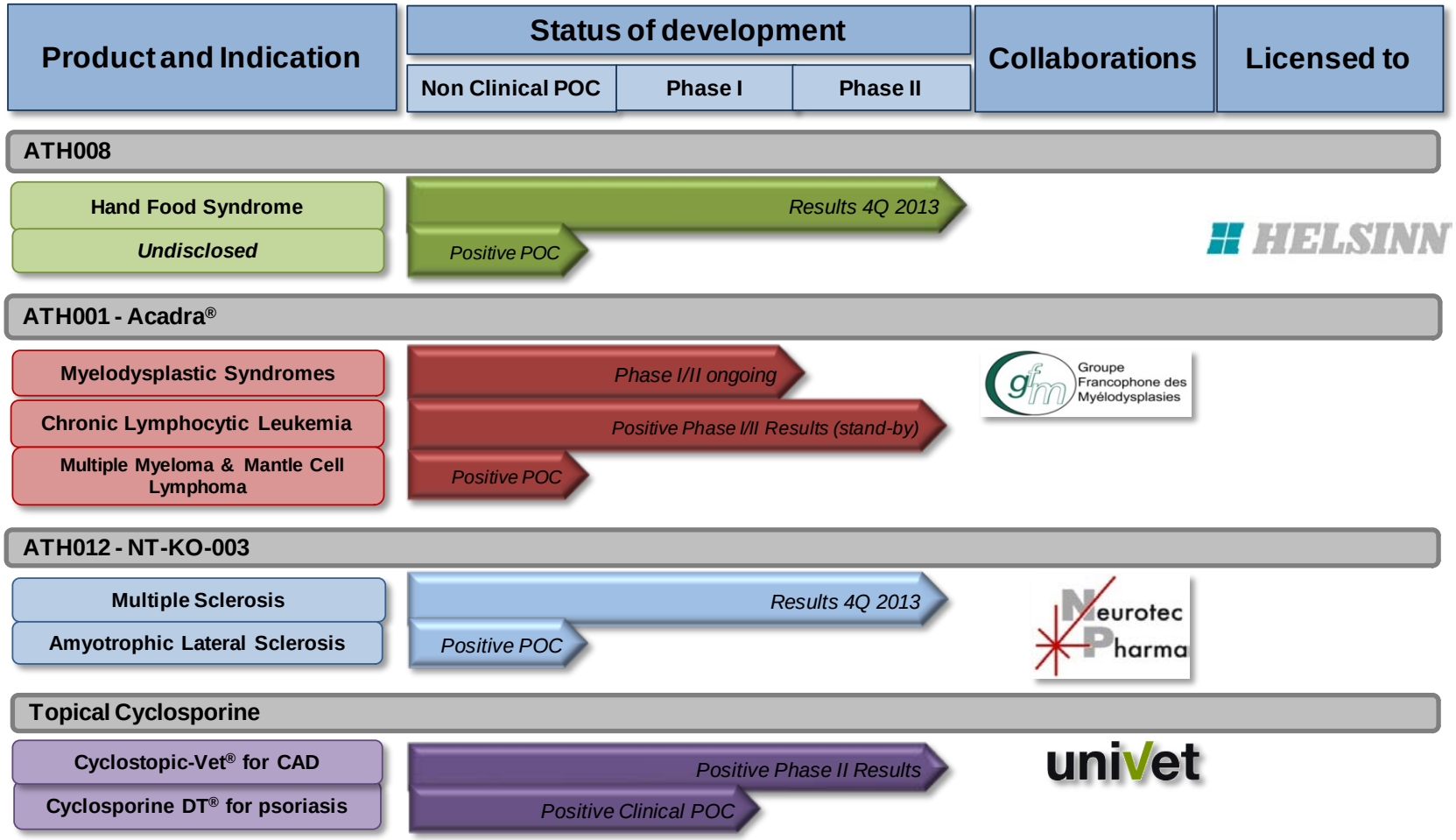
3. Partnering Opportunities

- ✓ NeuroAdvan is a joint program between Advancell & Neurotec Pharma.
- ✓ Our goal is to develop NT-KO-003 to Clinical Ph 2a in Multiple Sclerosis.
- ✓ Advancell and Neurotec are co-funding this program.
- ✓ We aim to partner the product after clinical proof of concept to a pharmaceutical company that can complete development to market and commercialize the product worldwide.

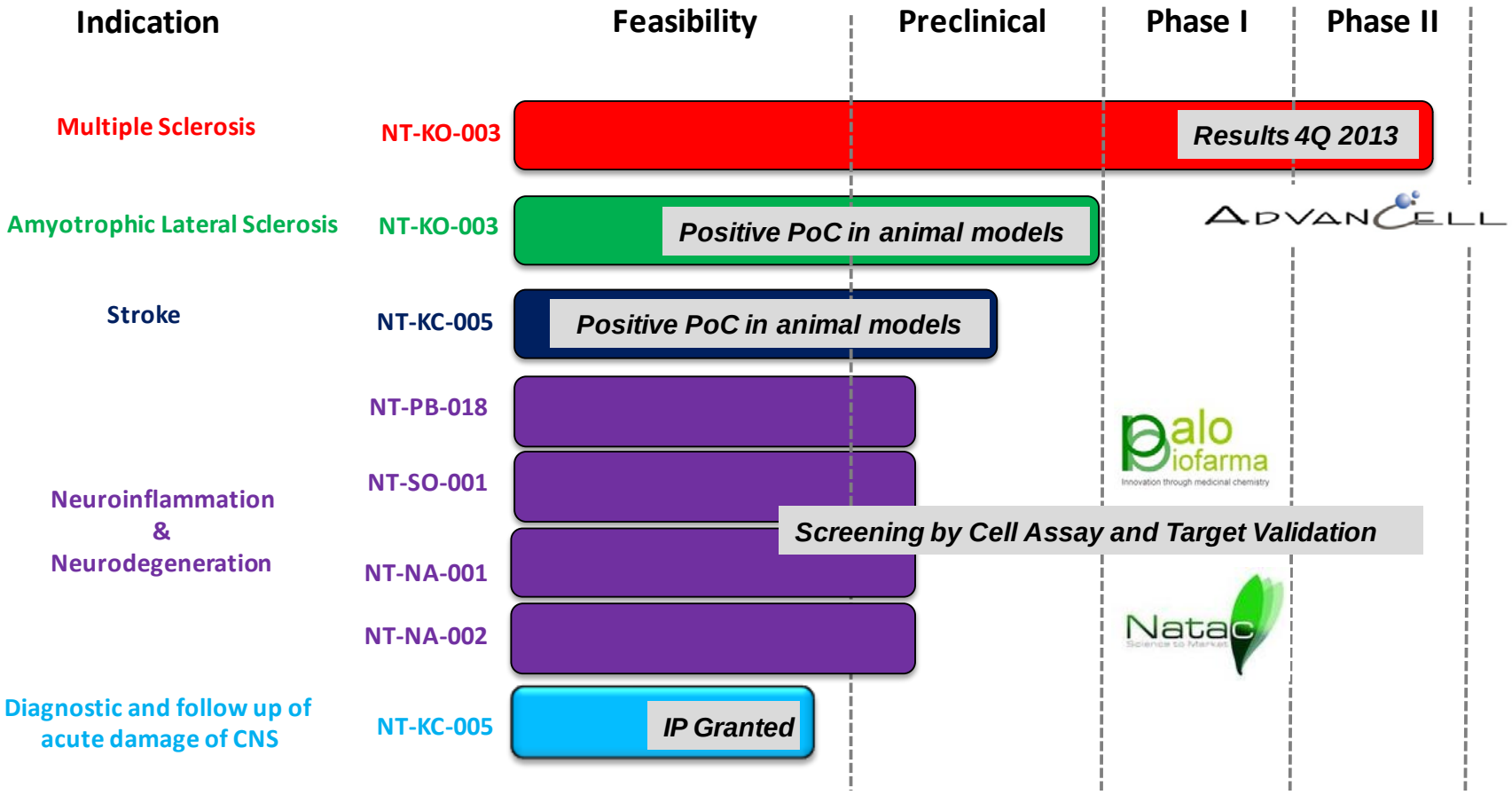
- ✓ At ADVANCELL we *i)* "cherry pick" intellectual property and know-how from the European academic environment and *ii)* develop the selected programs to clinical Phase 2, with the aim to *iii)* out-license these products to pharmaceutical companies that will complete development to market and commercialize the product worldwide.
- ✓ We outsource development activities to highly specialized companies, clinicians and scientists that work as a virtual team in a cost-efficient and quick-to-market manner, avoiding overrun caused by large non-specialized structures.
- ✓ With this strategy we put in value highly qualified scientific and clinical knowledge from our academic environment, allowing these ideas to become real products for the treatment unmet needs.
- ✓ We generate revenues through license agreements (upfront, milestones and royalties) to make our business sustainable and profitable for our investors.
- ✓ Located in Barcelona, founded in 2001 and privately owned, our Board and Management team has strong academic, financial and pharmaceutical experience.

ADVANCELL Clinical Pipeline 2013



- Neurotec is a biopharmaceutical company located in the Barcelona Science Park, focused on the development of new treatments for Central Nervous System (CNS) diseases with neuroprotective and anti-inflammatory effects.
- Founded in 2006 as a spin-off of the University of Barcelona, Neurotec works with accepted animal models of CNS diseases and primary cell culture and cell lines from neurons and glia. All standard technological tools in neuroscience are also available in the company.
- Neurotec employs 6 staff, all of them highly specialized in neuroscience.
- Neurotec business model is based on the reprofiling of drugs for their development in CNS up to Clinical Phase I-II with the aim to increase their value and transfer them to third parties by out licensing.

Neurotec Non-clinical and Clinical Pipeline 2013



NT-KO-003 Target Indications

1. Treatment of **Multiple Sclerosis** with the aim to be positioned as a disease modifying therapy → Phase 2a ongoing

2. Might have a role also in the treatment of **Amyotrophic Lateral Sclerosis** → Non-clinical proof of concept

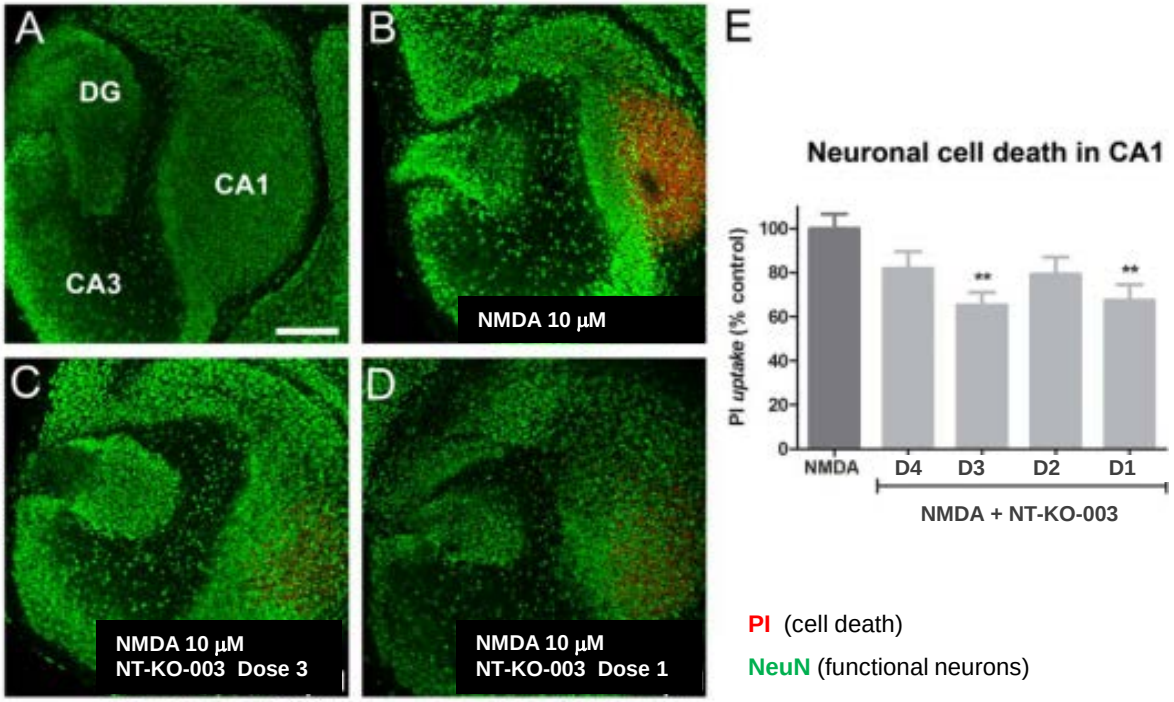
NT-KO-003 Mechanism of Action

- ✓ Neuroprotective
- ✓ CNS anti-inflammatory (glial mediated)
- ✓ Anti-demyelinating / Remyelinating (*studies ongoing*)
- ✓ Does not induce immunosupression

⇨ Molecular Target is a **K-ATP channel**

NT-KO-003 Mechanism of Action (I)

- ✓ Neuroprotective



PI (cell death)

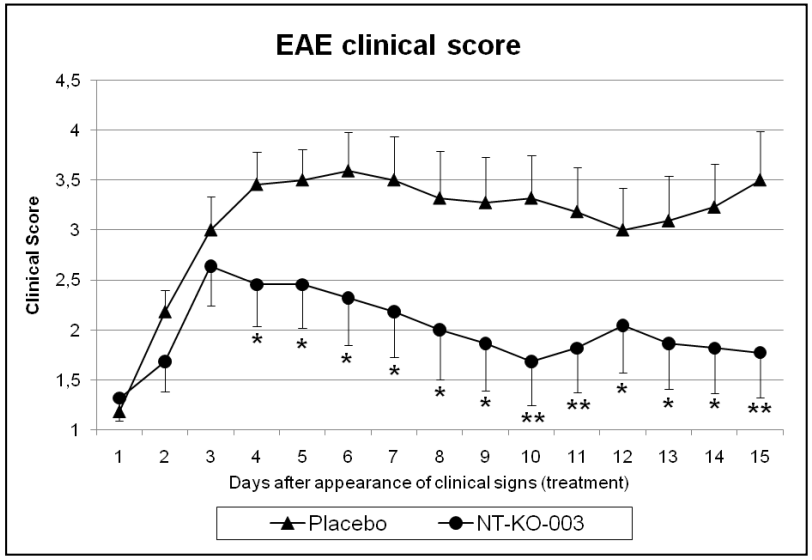
NeuN (functional neurons)

NT-KO-003 causes neuroprotection in organotypic cultures

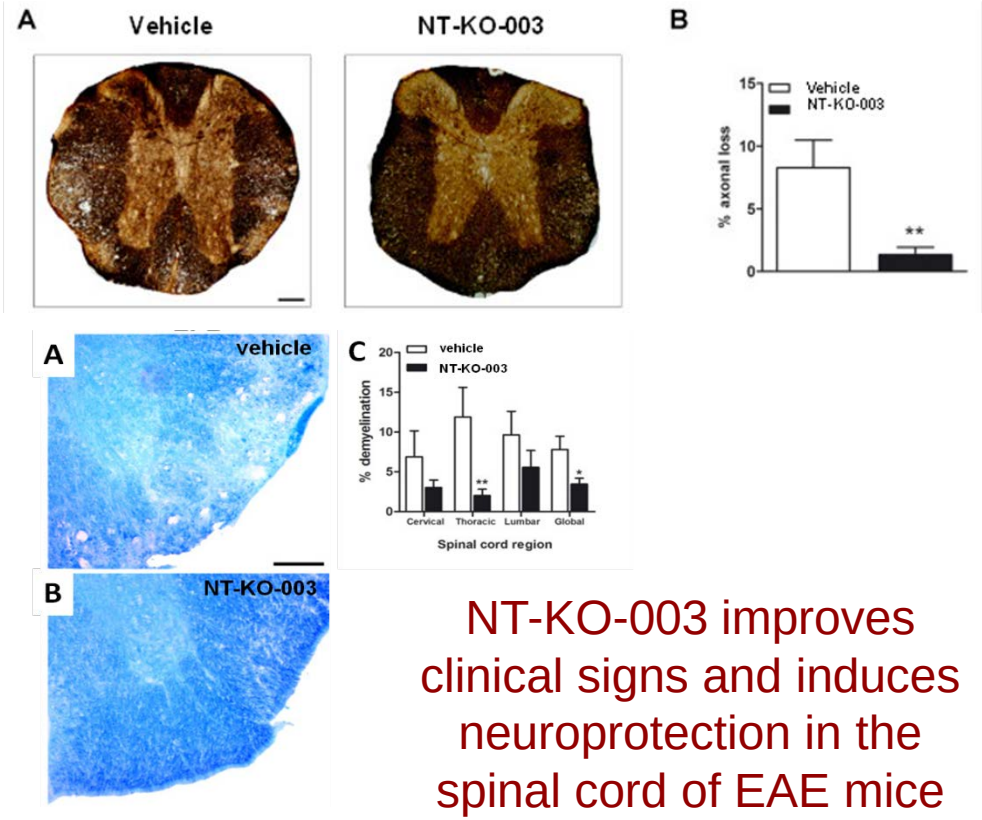
NT-KO-003 effectively inhibits neuronal death induced by NMDA insult in murine hippocampal slice cultures (at high but also at low doses).

NT-KO-003 Mechanism of Action (II)

- ✓ Neuroprotective



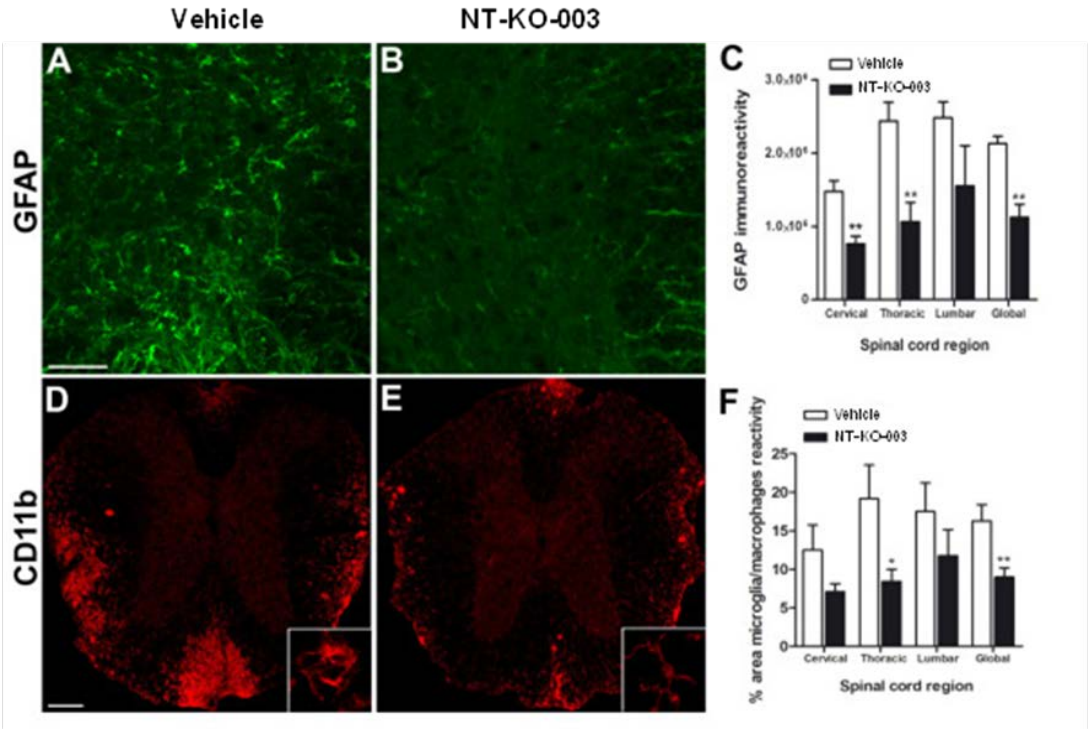
Daily clinical "Score" in the group treated orally with **NT-KO-003** (circles) compared with animals treated with placebo (triangles) from first symptoms to end of treatment. At histological level, **NT-KO-003** decreases axonal loss and improves myelin protection in EAE mice.



NT-KO-003 improves clinical signs and induces neuroprotection in the spinal cord of EAE mice

NT-KO-003 Mechanism of Action (III)

- ✓ CNS anti-inflammatory (glial mediated)

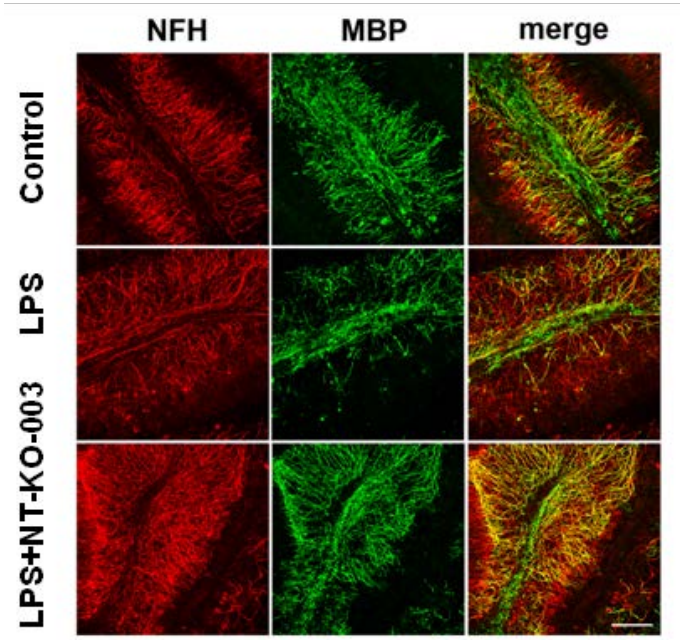


NT-KO-003 reduces glial reactivity in the spinal cord of EAE mice

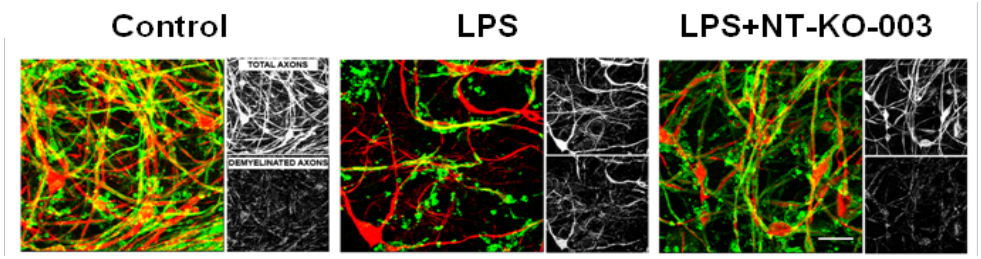
GFAP immunostaining of spinal cord sections vehicle- and **NT-KO-003-**treated EAE mice (A and B, respectively). Results show a decrease of GFAP intensity in NT-KO-003 treated animals (C). CD11b immunolabeling of spinal cord sections of vehicle- and NT-KO-003-treated EAE mice (D and E, respectively) allows the identification of reactive microglia/macrophages. Results show a smaller area of reactivity in NT-KO-003 - treated mice when compared to vehicle treated EAE mice (F).

NT-KO-003 Mechanism of Action (IV)

- ✓ Anti-demyelinating / Remyelinating (*studies ongoing*)



heavy neurofilament (NFH)
myelin basic protein (MBP)



NT-KO-003 prevents demyelination in organotypic cultures

NT-KO-003 preserved myelin structure and decreased axonal loss in LPS-mediated demyelination murine model of organotypic cerebellar cultures

NT-KO-003 Differential features

Feature	Competitive advantage
Oral	Most approved drugs in MS are not oral bioavailable
Once-a-day pill	Better compliance (chronic treatment, young adults)
Safe and well tolerated	• Avoids tolerability concerns of classic MS drugs • Better compliance (chronic treatment, young adults) • Permits use in combination
New MOA	• Targets the disease • Does not cause immunosupression • Permits use in combination
Small molecule	Attractive COGs, much below monoclonal antibodies

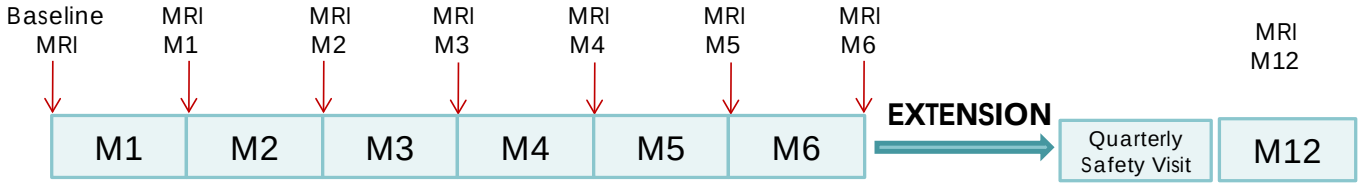
NT-KO-003 Development Status (I)

- ✓ Drug Substance scaled-up to commercial batch size
- ✓ Drug product scaled-up to 150.000 tablets batch size
- ✓ ICH stability studies ongoing (current shelf-life 36 months)
- ✓ The molecule has been marketed for non-CNS indications (acute and chronic use) at much higher doses.
- ✓ Toxicological & Pharmacological profile is well documented and covers adequately the current requirements to support a clinical trial of chronic duration (Guideline ICH M3 (R2)). Adverse Events of NT-KO-003 are already known from the clinical experience with higher oral doses.
- ✓ Non-clinical proof of concept and mechanism of action package available.

NT-KO-003 Development Status (II)

A **Phase 2a** multicenter double blind study to evaluate the efficacy and safety of low doses of oral NT-KO-003 vs placebo in Relapsing Remitting Multiple Sclerosis (RRMS) patients (ClinicalTrials.gov Identifier: NCT01428726)

Six months treatment with optional 12 months extension treatment under the same arm of the study. Safety and Efficacy (MRI) end-points.



The study is conducted in of 17 sites in Spain and Germany with a total of 103 patients.

Recruitment was completed on 15-March-2013. Results are estimated Q4 2013.

NT-KO-003 IPR Protection

- Patent applications covering worldwide market
- Rights extended up to ≥ 2029
- Patents of use in the indications (the molecule is out of patent)

NT-KO-003 Pitfalls & Risks

Pitfall/Risk	Strategy
Patents of use are weak in some territories	Patent strategy in layers. New IPR related to formulation and procedures.
Off-label use (the molecule has been marketed for another indication)	Not anymore marketed for non-CNS indications in most markets. Dose differs in orders of magnitude Formulation-IP strategies.
Efficacy of new MOA in treatment of MS	BG-12 (Tecfidera®, Biogen) already demonstrated that neuroprotection is an effective MOA to treat MS
Phase 2a study duration (6 months)	12 months data will be available for an important number of patients. Validated MRI variables of neuroprotection are being measured.

Partnering Opportunities

- ✓ Advancell and Neurotec Pharma aim to partner the program after Phase 2a.
- ✓ Our preferred partner is a company able to effectively complete the development of NT-KO-003 and competitively market the product.
- ✓ We seek a customary licensing transaction – upfront, milestones and royalty.
- ✓ Global rights still available
- ✓ The results of the Phase 2a study will be presented to a selected group of companies at the JP Morgan Conference in San Francisco (13-16 January 2013). If your company wants to be included in this group of companies please let us know.

Thank you

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