Programa Cooperación Farma-Biotech

Neurociencias

G79

A Neuroprotective Therapy

bionure

Biomedicine heading to future

Barcelona, 15 de febrero 2011

CataloniaBIO
Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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1. The Company

Bionure is a biotech company that was born in **2009** with the aim of developing new therapies and diagnostic tools for neurological diseases with special focus in Multiple Sclerosis and Glaucoma

Bionure is an Spin-Out from prestigious research centres with strong expertise in translational research:

CLÍNIC BARCELONA Hospital Universitari

The Hospital Clinic of Barcelona is the medical school of the University of Barcelona and one of the most prestigious medical centres in Europe for medical care, research and innovation in health care. www.hospitalclinic.org

IDIBAPS Institut d'Investigacions Biomèdiques August Pi i Sunyer

IDIBAPS is the research centre of the Hospital Clinic, with the support of the medical school of the University of Barcelona, the National Research Council CSIC and the Government of Catalonia. IDIBAPS focus in research and innovation in biomedicine. www.idibaps.org

CSIC Consejo Superior de Investigaciones Científicas

The national research council CSIC is the most prestigious research center in Spain in all areas of science and technology. www.csic.es

1. The Company - Founders

Dr. Pablo Villoslada, *Managing Partner*, CSO

MD by the University of Santiago Compostela and PhD in Neuroimmunology by the Autonomous University of Barcelona

Director of Neuroimmunology group at IDIBAPS – Hospital Clínic of Barcelona (http://www.idibaps.com/)

He has published more than 60 scientific articles

Inventor of 7 patents about the diagnosis and treatment of MS and other brain and retina diseases, some of them already licensed to other biotech companies (Digna Biotech, Progenika Inc..)

Member of several advisory boards for pharma or biotech companies (Roche, Novartis, Digna, …)

Member of the scientific committee of several international scientific societies and scientific journals (International society of Neuroimmunology, …)

Albert G. Zamora, *Managing Partner*, CEO

Pharmacist by the University of Barcelona, MBA by EADA (Barcelona), and master on corporate social responsibility (Stanford-ESADE)

Director of Strategic Marketing & Business Development of Hospital Clínic de Barcelona

More than 10 years of experience in strategic marketing and business development in pharmaceutical and medical devices industry.

Previous experience in two start-ups in biomedicine

Joaquin Uriach, Partner

Master in Law by the University of Barcelona and MBA by ESADE (Barcelona)

Secretary of the board of Uriach Corporation (http://www.uriach.com/indexe.html)

Vice-president of the Multiple Sclerosis Foundation (Barcelona)

Long-term experience in pharmaceutical industry

2. a)The Product – Therapeutic focus MS

Multiple Sclerosis (MS):

- Inflammatory and degenerative disease
- Chronic disease with no cure
- 2 Million people worldwide (white population: US, Canada, Europe)
- Most common disease in young adults
- Half of them will be in a wheel-chair after 20 years of disease
- Therapies costs: 10-40,000 $/patient/year
- Therapies are covered by national health systems and HMO

The MS market was 4,6 B$ in the 7 most important markets

…. And it is going to reach the 10,7 B$ by 2016.

MS has a significant health and social impact

2. a) The Product – Therapeutic focus Glaucoma

Neuro-Ophthalmology: Retinal diseases

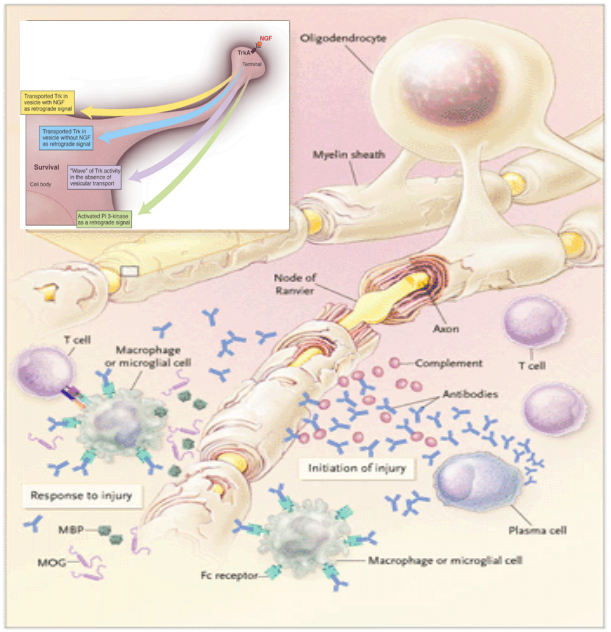
- The retina is part of the nervous system
- The main cause of blindness in Western countries
- Blindness is the second concern in terms of quality of life in the elderly after dementia
- Chronic diseases with no cure
- Glaucoma, Macular Degeneration, Diabetic Retinopathy
- The eye allows local ways of administration (e.g. collyrium)
- new imaging technologies are very accurate for monitoring disease progression and response to therapy
- Glaucoma is a neurodegenerative disease (*The eye's Alzheimer disease*)
- More than 60 Million people worldwide and more than 80M by 2020
- Current therapies only target high intraocular pressure

Glaucoma and blindness have a significant health and social impact

2. b) The Product – innovative mechanisms of action

The aim of Bionure is developing neuroprotective drugs by targeting the Neurotrophin (NGF, BDNF, NT3) pathway, and its receptors TrkA/B/C and p75:

- New approach for the treatment of brain and retina diseases
  - New mechanism of action: the pathway is well-known and it has been attacked by pharmas (Genentech, Amgen, etc.) in the past. However, there are still no therapies with this target in the market
  - Avoiding high selectivity for preventing side-effects and covering common pathways for neuroprotection
- Neuroprotective drugs
  - Drugs that prevent neuron death after injury (inflammation, ischemia, trauma, etc.)
  - Enhances recovery by natural mechanisms (remyelination)
- Oral administration and less side-effects because it do not impair the immune system function
- Combination therapy with current drugs: no competition



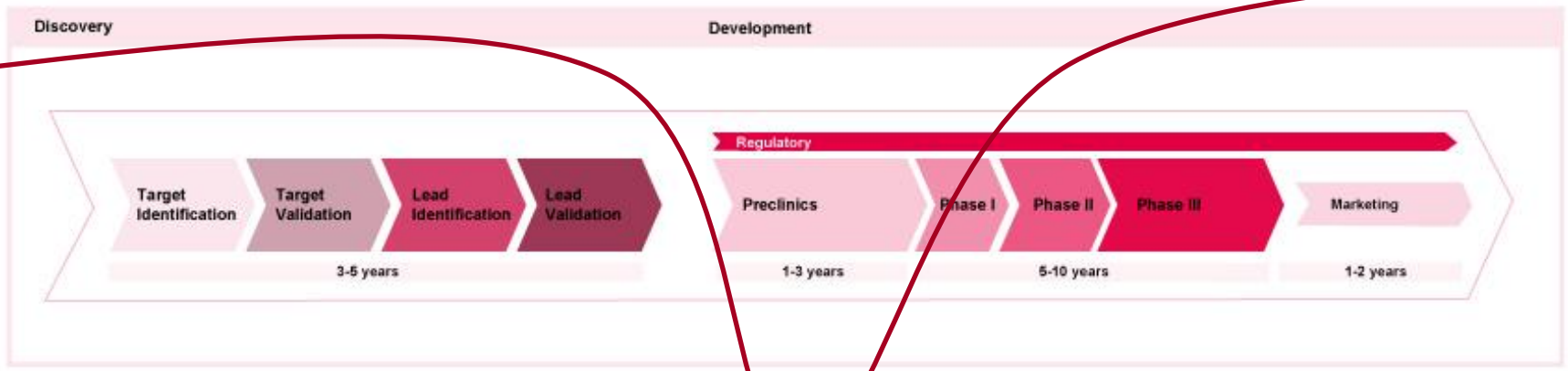
2. c) The Product –Differential features facing the market

Current therapies	Bionure
Single target	Multiple targets
Only target inflammation	Targeting neuroprotection and regeneration
Only benefiting patients in the early to medium phase of the disease	Benefiting patients in all stages
Do not prevent brain damage	Preventing brain damage
Do not prevent neurodegeneration	Preventing neurodegeneration
Limitation for combination therapy due to side-effects	Suitable for combination therapy
Injectable	Orally available

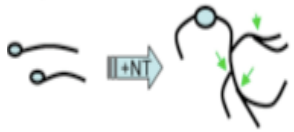
Current therapies for glaucoma are **intra-ocular pressure (IOP) lowering drugs** (decrease the intra-ocular pressure) and they are useful only in the one third of patients with high IOP

They have limited efficacy in slowing disease progression.

Bionure's Business Model



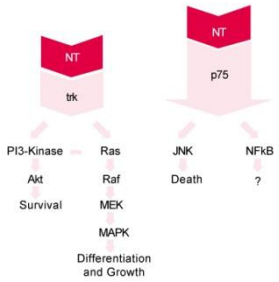
2. d) Current status of development



Neurotrophic assay
PC12 cell line

Survival assay (oxidative stress)
RN22 cell line

Signaling assay
NGF receptors



Animal models
MS and Glaucoma

- We have screened more than 5,000 small chemicals from 2 combinatorial libraries
- Compound were selected based in their **effect in vitro**
- Target/pathway (TrkA) specificity was used for filtering compounds
- Candidates were identified after obtaining the PoC **in vivo** in animal models of MS and Glaucoma

- Moreover, we have performed a Medical Chemistry analysis that defined:
- We have identified up to 9 hits with in vitro and in vivo activity
- We are currently performing comparative studies and candidate optimization through computational modeling
- We plan to identify new candidates and perform regulatory studies that are going to define the best candidate for entering the clinical phase

2. d) Current status of development

Bionure candidate G79 2010-2011

- **MoA: Signaling, mechanism of action and molecular validation studies**
- **Efficacy in vitro (human cell lines)**
- Chronic treatment in vivo EAE models
- Neuroprotection effect in vivo EAE models
- Protein-binding studies and off-target effects study
- **Medical Chemistry Studies**
- Therapeutic performance studies (interaction with other possible target in silico studies)
- Pharmacology: ADME in vitro & in vivo, cardio (Ikr, QT) respiratory, SNC
- **Combination therapy with current treatments for MS**
- Non-regulatory toxicology

"Hit to lead" approximation 2011-2012

- Medical chemist & computational studies
- Comparative with other molecules in development
- Candidate selection

Same pre-clinical non regulatory studies

Candidate selected (best approximation) 2012-2014

- Side-effects screening: neuropathic pain, heart toxicity
- Toxicology: single dose in different species, repeated doses (2w), chronic (6m & 9m)
- GMP production & IMD
- Phase I – first human studies

2. e) IPR protection

- 2 patents filled to the European Office by the academic institutions covering 6 molecules, have been licensed to Bionure
  - 1. "New 3-oxopiperazinium derivatives agonists of nerve growth factor and their use as medicaments". Inventors: Pablo Villoslada Diaz, Beatriz Moreno, Angel Messeguer, Joaquin Messeguer, Gloria Navarro. **EP2009 169036.2** Priority date: August 31 2009. –Extension en August 2010: **PCT/US2010/47405**
  - 2. "New peptoids agonists of nerve growth factor and their use as medicaments". Inventors: Pablo Villoslada Diaz, Beatriz Moreno, Angel Messeguer, Joaquin Messeguer, Gloria Navarro. **EP2009 09169045.3** Priority date: August 31 2009. –Extension en August 2010: **PCT/US2010/47407**

- Bionure has filled a new patent in the US by August 2010 covering 3 new peptoids (G79, G80, G81) and several indications for brain and retina diseases: **US61/378,823**

- **Bionure** trademark was registered by March 29th 2010 #**1036701** for 10 years in the US and Europe.

2. f) Pitfalls & Risks to be considered

- Neuropatic pain
- Interactions
- ADME – Blood Brain Barrier
- Toxicology

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3. Availability for cooperation

- Corporate – investor 2nd round (2012)
- Project investment – benefit sharing
- Other neurological indications IP rights – licensing
  - Alzheimer
  - Parkinson
  - ELA
- *Co-development*

bionure

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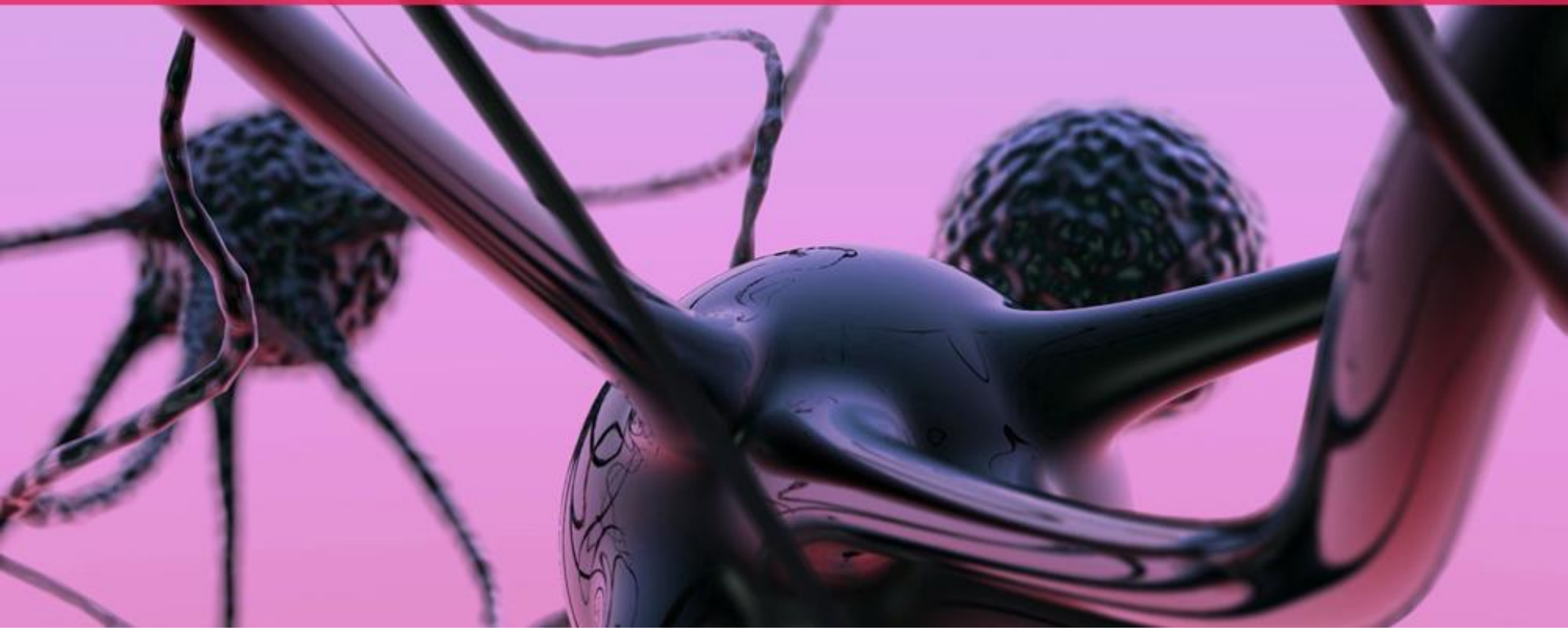

Thanks for your attention

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