MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

Acción experimental para el fomento de la cooperación entre compañías farmacéuticas y empresas y grupos de investigación en el ámbito de la biotecnología

XIII Encuentro de Cooperación Farma-Biotech

Martes, 20 de octubre de 2015

La jornada tiene por objeto estimular la cooperación entre compañías farmacéuticas nacionales e internacionales, empresas españolas de biotecnología y grupos de investigación, en torno al desarrollo de nuevos medicamentos innovadores.

La iniciativa diseñada por FARMAINDUSTRIA se propone a través de esta jornada que empresas españolas y grupos de investigación de centros especializados, previamente seleccionados, expongan, ante las compañías farmacéuticas interesadas, productos en desarrollo con el potencial suficiente (innovador, eficaz, protegido) que pueda representar una oportunidad de cooperación para ser explorada por ambas partes.

Tras un cuidadoso estudio de necesidades expresadas por las compañías farmacéuticas y del estado de desarrollo de las investigaciones en curso en las empresas biotecnológicas y los grupos de investigación, se han seleccionado ocho propuestas para que realicen su presentación en la jornada del martes día 20 de octubre en Barcelona.

Por parte del sector farmacéutico asistirán directivos de I+D y Desarrollo de Negocio de las compañías que han expresado su interés en participar. El grado de información manejado durante la jornada se clasifica como "no confidencial" por lo que no se requiere ningún acuerdo previo al respecto.

La jornada se configura por lo tanto como un foro individualizado no abierto a terceras partes, y en donde se desea generar un clima de interacción suficiente que permita identificar el valor añadido derivado del intercambio de información entre demanda y oferta, con suficiente contenido diferencial e innovador en el ámbito de las nuevas terapias y los medicamentos avanzados.

Para cualquier duda o aclaración sobre esta jornada por favor contactar con:

Amelia Martín Uranga

amuranga@farmaindustria.es

Tfno. 915159350

Agenda

La organización de la jornada pretende dar énfasis tanto a las presentaciones como a la interacción personal entre los asistentes, de acuerdo con la siguiente agenda:

08:45 09:15	Recepción, contactos informales, café	Estado de Desarrollo	Ponente
09:15 09:30	Bienvenida y presentación de la jornada		Farmaindustria
09:30 10:00	*SOM3355, un candidato prometedor para el tratamiento de la enfermedad de Huntington*	Iniciando Fase IIa	***Santiago Esteva*** SOM Biotech
10:00 10:30	*Nuevos bloqueadores de canales de Calcio para el tratamiento del dolor neuropático*	Prueba de concepto celular	***Cristóbal de los Ríos*** I.I.S. H. la Princesa
10:30 11:00	*Nuevos compuestos con estructura multitarget para tratamiento de enfermedades neurodegenerativas*	Prueba de concepto celular	***Rafael León*** I.I.S. H. la Princesa
11:00 11:30	*ORY-2001, un avance epigenético en el tratamiento de la enfermedad de Alzheimer*	Iniciando Fase Clínica I	***Emili Torrell*** ORYZON Genomics
11:30 12:00	Café, refrescos, contactos directos		
12:00 12:30	*LP226A1 para el tratamiento de la enfermedad de Alzheimer*	Preclínica regulatoria	***Vicenç Tur*** LIPOPHARMA
12:30 13:00	*Biomarcadores en sangre para el diagnóstico temprano de la demencia*	Validada Fase 2	***Katrin Beyer*** I.I.S. Germans Trias i Pujol
13:00 13:30	*BN 201: programa avanzado para el tratamiento de la neuritis óptica aguda*	Completada preclínica regulatoria	***Gerard Caelles*** BIONURE
13:30 14:00	*Uso de chaperonas farmacológicas para el tratamiento de ciertas enfermedades raras*	Completadas pruebas preclínicas	***David Cotan*** PRONACERA Th.
14:00- en adelante	Aperitivos y refrescos. Contactos directos		

Todas las presentaciones se harán en español, si bien la documentación escrita se dispondrá en inglés para facilidad de circulación interna entre los órganos de las compañías internacionales

Lugar de celebración: **Delegación de Farmaindustria en Barcelona. Avda. Diagonal nº 361. 3ª**
Fecha: **Martes día 20 de octubre de 2015**

La plataforma tecnológica Española Medicamentos Innovadores, cuenta con apoyo financiero del Ministerio de Economía y Competitividad (PTR-2014-0337)

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

SOM BIOTECH

PROFILE

SOM Biotech is a clinical-stage biopharmaceutical company established at the Barcelona Science Park with the mission to discover and develop new indications of already known drugs (repurposing) through a profitable private company committed to its shareholders, employees and society. Our work includes drug discovery, pre-clinical validation, industrial protection, human proof of concept and licensing. SOM Biotech has also special interest in rare diseases. The company's pipeline includes 1 program under Phase IIa (TTR Amyloidosis), 1 program ready to start Phase IIa (Huntington's disease) and three in preclinical stages (Benign Prostatic Hyperplasia, Alzheimer and Glioblastoma).

SPEAKER

Santiago Esteva, Business Development Manager, holds a PhD cum laude in Biology from the University of Barcelona. His research was focused on physiological states under hypoxic conditions. When he finished his academic period, he joined the Clinical Research sector and carried out different management tasks in CROs for several years. He is currently in charge of the Business Development at SOM Biotech. Santiago has also attended Masters Courses in Clinical Trials and Pharmaceutical Marketing.

esteva@sombiotech.com

PRODUCT

SOM3355, a promising repurposed candidate intended for the treatment of Huntington's disease

MECHANISM OF ACTION

It has been demonstrated that SOM3355 inhibits striatal Vesicular Monoamine Transporter-2 (VMAT-2 inhibitor) and ultimately, it reduces dopamine transmission selectively in the CNS.

TARGET INDICATIONS

Huntington's disease (chorea movements associated to Huntington's disease). Also potential activity in Tourette's syndrome, Tardive dyskinesia and Hemiballismus. All are defined as rare diseases in the neurological area.

CURRENT STATUS

- In vitro screening tests performed against tetrabenazine. Identification of VMAT-2 inhibitors. (SOM3355 and tetrabenazine showed a similar range of activity at nM level).
- In vivo experiment to study SOM3355 brain/plasma concentration ratio. Results showed that SOM3355 significantly penetrates the BBB.
- Phase IIa Proof of Concept in humans to be started during 4Q2015. Regulatory and clinical trial documentation ready to be submitted to Authorities.

INNOVATIVE ASPECTS

- There is only one symptomatic approved treatment for Huntington's disease: tetrabenazine.
- SOM3355 might represent a therapeutic alternative to this existing treatment. A clinical Phase II Proof of Concept study is expected to start in Huntington's patients during Q4-2015.
- SOM3355 is a potent inhibitor of VMAT-2 and for its primary indication it has been largely tested in vivo and safely administered to humans. As a repositioned drug it can bypass much of the early cost and time needed to bring a drug to market.

IPR

- A European patent was submitted protecting the use of SOM3355 in Huntington's disease. Afterward, this European Patent was extended as world-wide PCT. National phases will start next December 2015. In addition, the patent covers its synergic activity with other compounds (including tetrabenazine) and also different routes of administration and several dose regimes.
- Orphan Drug Designation (ODD) of SOM3355 for the treatment of Huntington's disease to be submitted to EMA and FDA during 2016.

PARTNERING OPPORTUNITIES

SOM Biotech business model is based in licensing and joint-venture agreements for the development of repositioned drugs. We are open to any type of agreement, from a full-sell of the project to a joint-venture for development.

SOM Biotech is willing to out-license SOM3355 program before or after the clinical Phase IIa. The deal structure would be: upfront, milestones and royalties. Alternatively, we would be open to deal with a company willing to co-fund the Phase IIa in order obtain a future first option to in-license the whole program.

Instituto de Investigación Sanitaria Hospital de la Princesa

PROFILE

La Princesa Institute for Health Research is committed to both promote innovation and facilitate the transfer of knowledge to the private sector in an effort to achieve significant public health benefits. Day after day 500 scientists work in their Hospital research laboratories located in Madrid . The Institute is really focused on translational neuroscience research in the fields of Neurotransmission, Pharmacological neuroprotection, Neurodegenerative and Neuropsychiatric disease.

SPEAKER

Cristóbal de los Ríos is PhD in Chemistry (Universidad Autonoma de Madrid). His current scientific interest is the drug R&D for nervous system diseases. He focuses on the discovery of new ligands for innovative biological targets, with high potency and selectivity. He has published more than 40 papers in MedChem journals and 4 patents. He has participated in a more than ten research projects, being the PI in 2 of them.

cristobal.delosrios@uam.es

PRODUCT

New non-L-subtypes Calcium channels blockers for applications on Nervous System Pathologies

MECHANISM OF ACTION

Twenty compounds were evaluated, possesing neuroprotective properties in in vitro models of neurodegeneration. They also blocked calcium channels, being the best blocker the 1-benzyl-5-methyl-3-(piperidin-1-ylmethyl)-1H-indole, named as ITH12657.

The new compounds, highlighting that called ITH12657, blocked voltage-gated calcium channel, with selectivity to those classified as non-L, that are mainly P/Q and N-type calcium channels. They reduced calcium entry stimulated by depolarization by about 30% in neuroblastoma cells, and 4 of them blocked calcium currents in bovine chromaffin cells efficiently.

The compound ITH12657 blocked calcium current by 40%, a blockade that was added to that elicited by nifedipine when this L-type calcium channel blocker was exposed to cells. Such blocked was masked in presence of toxines selective to non-L channels.

Due to the key role of voltage-dependent Ca2+ channels and their control of the cell Ca2+ levels in neurons, these compounds can regulate the Ca2+ overload described in several pathologies of the nervous system

TARGET INDICATIONS

Neuropathic pain, such as neurodegenerative (Alzheimer's, Parkingson's, Amyotrophyc Lateral Esclerosis), stroke, other types of pain, and epilepsia, so it can be used as medicines to treat these diseases.

CURRENT STATUS

- Two dozens of compounds synthesized possessing neuroprotective properties in several in vitro models of (cortical neurons, hippocampal slices, neuroblastoma cells) neuronal damage: exposure to the toxicants veratridine, glutamate, rotenone plus oligomycin A, and high K+ concentration. Most of them reduced calcium entry induced by 70 K+, measured with the fluorescent dye fluo-4AM in neuroblastoma cells.
- The best compounds blocked Ca current in chromaffin cells by patch-clamp. The most highlighted compound featured such blockade through non-L-type calcium channels.
- Chemical Synthesis: Subgram scale and salinization to improve water solubility.
- Cell culture-based In vitro assays: (a) Compounds blocked Ca2+ increase induced by depolarization in SH-SY5Y cells, (b) protected efficiently SH-SY5Y cells against a model of Tau hyperphosphorylation-dependent diseases, and (c) protected efficiently rat motor cortex neurons against a model of Ca2+ overload.
- Tissue preparations-based In vitro assays: Selected compounds protected rat hippocampal slices against a model of Ca2+ overload and excitotoxicity.
- Patch-Clamp experiments: Selected compounds blocked Ca2+ entry via voltage-dependent Ca2+ channels in chromaffin cells. The best one did not affect the cardiovascular-related L-type, but the P/Q and N-type Ca2+ channels, targets for the treatment of neurophatic pain.

INNOVATIVE ASPECTS

- There are no efficient or safe medicines to treat neurophatic pain, as well as for other types of both acute and chronic pains. The few medicines available show severe adverse effects and/or poor pharmacokinetic parameters (most of them are extremely polar substances), so they need to be administered by injection.
- There are very few calcium channels blockers targeting those named non-L. Moreover, the few ligands that block T-, N- or P/Q-type calcium channels are not selective, as most of them also block L-type channels. In addition, many of them are peptides or peptidomimetics, so they have a very poor blood-brain penetration, what limits their use in central diseases.
- The compounds presented in this proposal are low-molecular-weight molecules possessing potential decent pharmacokinetic parameters to be suitable for oral administration (log P, water solubility, pKa, etc)
- These compounds would not present cardiovascular-related side effects.

IPR

Patent status: P201500354. Priority date: 05/14/2015

PARTNERING OPPORTUNITIES

We search for companies with interest to license our research work, capable to further investigate its therapeutic applicability. In addition, we seek to extend this research to optimized compounds, evaluating their pharmacological activities in the models we skilled. Thus, we are open to make a collaboration with companies interested in granting our project to keep developing new calcium channel blockers.

Instituto de Investigación Sanitaria Hospital de la Princesa

PROFILE

La Princesa Institute for Health Research is committed to both promote innovation and facilitate the transfer of knowledge to the private sector in an effort to achieve significant public health benefits. Day after day 500 scientists work in their Hospital research laboratories located in Madrid . The Institute is really focused on translational neuroscience research in the fields of Neurotransmission, Pharmacological neuroprotection, Neurodegenerative and Neuropsychiatric disease.

SPEAKER

Rafael León, graduated in chemistry in 2001 obtained his Ph.D. in Organic Chemistry in 2006. After three postdoctoral stages at the UAM (Spain), University of Victoria (Canada) and University of Cambridge (UK) he was awarded the "Miguel Servet" project in 2012 to start his independent career. He obtained two major grants in Spain and the European CIG project from the ERC found. He has published 43 research articles and he has also presented 4 patents in the last three years.

rafael.leon@uam.es

PRODUCT

Compounds related to 3-alkylamine-1H-indolyl acrylate and their use for the treatment of neurodegenerative diseases

MECHANISM OF ACTION

Neurodegenerative diseases share many pathological pathways as abnormal protein aggregation, mitochondrial dysfunction, extensive oxidative stress and neuroinflammation.

Cells have an intrinsic mechanism of protection against oxidative stress, the Nrf2 transcriptional factor, known as the master regulator of redox homeostasis. Based on these common features we have designed a multitarget structure that can act as Nrf2 inducer and potent free radical scavenger.

The inclusion of both biological targets also induces an anti-inflammatory effect that can stop one of the most important hallmarks of these diseases. As result, it shows an interesting neuroprotective effect.

TARGET INDICATIONS

This family of products has been protected as potential treatments for neurodegenerative diseases including all mayor diseases as: Alzheimer's disease, Parkinson's disease, Huntington disease, amyotrophic lateral sclerosis, multiple sclerosis and ictus. The target of the named compounds is oxidative stress and the Nrf2-Keap1 antioxidant and anti-inflammatory pathway, thus, their indication can be extended for different inflammatory diseases as chronic obstructive pulmonary disease, for example.

CURRENT STATUS

- We have completed the design, synthesis and in vitro screening of a small chemical library of 32 compounds. The screening included: a) Nrf2 induction properties; b) free radical

scavenger effect; c) anti-neuroinflammatory properties and d) neuroprotective properties against three in vitro models of neurodegeneration.

- Currently we have evidences of the biological activities included. The combination of Nrf2 induction and anti-inflammatory properties will drive the reduction of oxidative and glial activation status of the patients reducing the neuronal loss.
- Our first achievement is the possibility to modulate the Nrf2 induction properties of these compounds. Moreover, our lead compound is able to scavenge free radicals five times better than melatonin and it showed a potent anti-inflammatory effect at 3 μM.
- It was able to protect more than 50 % neurons against two models oxidative stress, and 65 % neurons against okadaic acid. Finally, we have performed hepatotoxicity test in HepG2 cells without seeing any toxicity up to 100 μM.
- We have also evidences of a reduction of the inflammatory response induced by lipopolysaccharide in C57 mouse. In vitro test of this compound have also demonstrated the capacity to reduce neuronal death in several models of neurodegeneration.
- We are currently planning the proof of concept in a transgenic model of Alzheimer's disease and a model of multiple sclerosis. Finally, this compound has demonstrated a very good safety profile in HepG2 cells (hepatotoxicity model).

INNOVATIVE ASPECTS

- During the last two decades, the selected targets where, mainly, the formation of protein aggregates and / or the decrease of neurotransmitter levels. Taking into account that those hypotheses failed to bring up a disease-modifying drug, our approach is the use of novel targets.
- Currently, there is no treatment for most of the degenerative diseases or they are not effective. In addition, drugs that are now in clinical trials are directed to the same targets used before, and almost all of them are not demonstrating effectiveness. The compounds here proposed have been designed specifically to reduce oxidative stress and neuroinflammation for the first time.
- These two pathological hallmarks are increasingly considered the triggers of the neurodegeneration process. For the first time, we will be able to develop an early treatment for Alzheimer's disease able to stop the disease advance.
- The design of this family of compounds was based on common pathological pathways described for different neurodegenerative diseases. All derivatives are powders obtained in two simple synthetic steps and easily scalable. We have obtained 32 products in high yields and with high purity (> 99.99 %) that have been screened in six different in vitro pharmacological tests.

IPR

The core structure was not known; therefore, we have protected the main core and its possible derivatives, its synthesis and biological activity. We have also protected its use as drugs for neurodegenerative diseases with 19 claims. Application number: P201400810, Priority date: 15/10/2014, Country of protection: Spain.

PARTNERING OPPORTUNITIES

Our interest of collaboration with pharmaceutical industry is to further develop this family of compounds. First, to perform the in vivo proof of concept of the lead compound and, second to optimize the activities to generate a drug candidate. We also are looking for biopharmaceutical companies interested in licensing the compounds.

Oryzon Genomics, S.A.

PROFILE

Oryzon is a private clinical stage biopharmaceutical company that discovers, develops and plans to commercialize innovative epigenetic-based therapeutics in oncology and neurodegenerative diseases. Oryzon has built a proprietary product platform and will continue to create small molecules focused on certain classes of enzymes in the field of histone lysine methylation and demethylation, including Lysine-specific histone Demetylase-1-Inhibitors (LSD1), other lysine demethylases (KDMs) and lysine methyltransferases (HMTs).

SPEAKER

Emili Torrell, Director Business Development has a A bachelor's degree in Veterinary Sciences from the Autonomous University of Barcelona, MBA from ESADE and PDG from IESE. He also earned a Master's in Patent Documentation from the University of Barcelona. He began his career in the pharmaceutical industry in 1990 as Business Development Manager at Prodesfarma. Later on, he specialized on the international side as International Product Manager there and, after that, as International Marketing Manager with Almirall. Starting in 2004, he served in the position of Senior Licensing Manager at Laboratorios Dr. Esteve, and in February 2007, he joined Oryzon as Director of Business Development.

etorrell@oryzon.com

PRODUCT

ORY-2001: A breakthrough epigenetic approach in Alzheimer's disease and other neurodegenerative disorders.

MECHANISM OF ACTION

- ORY-2001 is an small molecule orally bioavailable with good BBB permeability and safety profile in the regulatory tox studies performed in rats and dogs and has a high TI. It has demonstrated in innovative non transgenic mouse models that it stop cognitive impairment and memory loss.
- ORY-2001 is a LSD1-MAOB dual inhibitor. LSD1, Lysine Specific Demethylase-1, is a chromatin modulator that demethylates primarily H3K4 and, in CNS, has been involved in the regulation of expression of neuronal genes and neurogenesis; MAOB, Monoamino Oxidase B, plays an important role in the catabolism of neuroactive and vasoactive amines in CNS and peripheral tissues and is responsible for dopamine degradation. MAOB is a well known target for Parkinson's Disease and has been explored in AD.
- Besides the current paradigms of the Amyloid and Tau hypothesis, the etiology of AD has been suggested to be connected to a variety of biological malfunctions including synaptic dysfunction, oxidative stress, inflammation processes and others. Many of them have an epigenetic causal component, and the influence of epigenetic control on the onset of neurodegenerative diseases has been well documented in studies with identical siblings.

- Different chromatin regulator complexes play an important role regulating neuronal gene expression during development and in adult neurons. One of the functional cores of this complex is formed by the histone demethylase LSD1, this chromatin modulator is frequently accompanied by the co-repressor CoREST, the histone deacetylases HDAC1/2, Myelin Transcription Factor 1 (MyT1), together with REST and others.

TARGET INDICATIONS

Treatment of neurodegenerative diseases, including Alzheimer's (AD), Parkinson's, Huntington's and other CNS disorders.

CURRENT STATUS

- The near term inflection points for the ORY-2001 program are to complete the IND package by Q4 2015, and file the IND/CTA by year end 2015. The Phase I program is intended to be focused in both the US and EU. The clinical development will enter Phase II in 2016.

INNOVATIVE ASPECTS

- The therapeutic approach of ORY- 2001 focuses on stopping cognitive and memory capabilities of patients suffering Alzheimer unlike the current available alternatives in the marketplace which address the management of symptoms but do not stop the disease.
- The neuroprotection evidences obtained so far anticipate the value of ORY-2001 in the treatment of AD as well as other neurodegenerative disorders. The Alzheimer's Drug Discovery Foundation has awarded multiple grants to Oryzon to help fund its development.
- In different animal models, pharmacological oral LSD1 inhibition stops cognitive impairment and memory loss and consequently ORY-2001 is an experimental drug that proposes a novel disease modifying option for a set of neurodegenerative disorders.

IPR

Patents applied internationally.

PARTNERING OPPORTUNITIES

The split of commercial territorial rights with the partner in return to a significant contribution in the clinical development is considered the preferential collaboration scenario. Oryzon is open to consider other models of collaboration.

LIPOPHARMA

PROFILE

Lipopharma is a pioneering, science-driven biopharmaceutical company that focuses on the discovery, rational design and initial clinical development of a new generation of medicines associated with a novel therapeutic approach: Membrane Lipid Therapy (MLT). Instead of directly targeting intracellular proteins, MLT-based molecules regulate the structure and function of cell membrane lipids and their associated proteins.

SPEAKER

Vicenç Tur. CEO. As co-funder of Lipopharma, over the last 7 years he has significantly contributed to the consolidation of an academic spin-off into a sound biopharmaceutical company with a promising pipeline of innovative products with potential applications in areas such as cancer or CNS. Economist by training, he holds an MBA from Stirling University (UK) and his previous professional career has been in a financial institution (Bank of Ibiza) and at the Confederation of Industries in the Balearic Islands (CAEB) as chief economist.

v.tur@lipopharma.com

PRODUCT

LP226A1 for the treatment of Alzheimer's disease

MECHANISM OF ACTION

LP226A1 is a modified natural fatty acid with highly specific incorporation into neurons due to the specific omega-3 transporters present in neuronal membranes. Our data indicates that the main mechanism of action is the inhibition of Tau phosphorylation and as a consequence the normalization of a number of altered molecular markers of Alzheimer's disease including the loss of Aβ amyloid load, activation of protective autophagy and synaptogenesis.

LP226A1 is a potent dose-dependent inhibitor of Tau phosphorylation (both in vitro and in vivo) as determined in differentiated SH-SY5Y cells and in brain samples of transgenic 5xFAD mice with Familiar Alzheimer´s Disease).

TARGET INDICATIONS

Alzheimer's disease.

CURRENT STATUS

- LP226A1 is currently in preclinical stage. A regulatory preclinical package is scheduled to be initiated within 2015.

INNOVATIVE ASPECTS

- Administered orally, this modified DHA shows significant disease modifying capacity in two different animal models (mice and flies).
- Treatment of 5xFAD mice with LP226A1 (15 mg/kg daily for 3 months) demonstrated a recovery of cognitive abilities as determined by a computer-assisted-radial maze exercise. This positive behavioural effect correlated with recovery of healthy brain biomarkers as

restoration of neurogenesis and synaptic protein expression (synaptophysin and SNAP25) in the hippocampus. Concomitant with these effects a loss of the total brain Aβ amyloid load was observed.

- In addition, in vitro studies demonstrated the capacity of LP226A1 in restoring the viability of SH-SY5Y cells in cell culture intoxicated with Aβamyloid peptide together with significant increases in markers of protective autophagy.
- As happens with DHA, LP226A1 crosses the BBB and preferentially incorporates into grey matter neuronal synapses through the activity of a number of proteins that are highly expressed in neuronal membranes (FATs, FABPs, FATPs).
- In preliminary safety studies in different animal models (mice and flies) LP226A1 has shown a clean safety profile, very similar to DHA, with no toxicity signs seen at therapeutic and higher doses.

IPR

Neurodegeneration indications of LP226A1 are protected by one global patent family that has already been granted in USA, Japan, Russia, Mexico and Spain. National phases in the rest of major markets are currently ongoing.

PARTNERING OPPORTUNITIES

Lipopharma is interested in exploring collaborations with pharmaceutical companies in order to complete the clinical development of LP226A1 in AD and, eventually, commercialize the compound globally. Our main objective is to bring the product to market as fast as possible

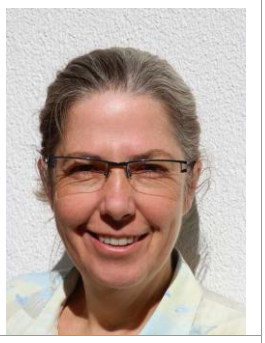
Health Sciences Research Institute "Germans Trias i Pujol"

PROFILE

Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol

The main goal of our research group is the identification of peripheral biomarkers for the early and differential diagnosis of Lewy body disorders. Our findings are based on genomic and transcriptomic studies, especially in post-mortem brain samples with an exhaustive neuropathological diagnosis. One of our most important achievements has been the identification of a molecular subgroup of dementia with Lewy bodies published in 2010 in Brain.

SPEAKER



Katrin Beyer, PhD, obtained her MSc degree in Biochemistry in 1988 and her PhD in Molecular Genetics in 2003. Twenty years ago she started working in research on genetics of Alzheimer disease. She has worked for 16 years in the department of Pathology of the University Hospital Germans Trias i Pujol where she expanded her research to other neurodegenerative diseases, such as Lewy body disorders.

kbeyer@igtp.cat

PRODUCT

Blood biomarkers for the early diagnosis of dementia with Lewy bodies

MECHANISM OF ACTION

"Biomarker 1" consists of the determination of various transcripts of certain gene (gene A) in blood of patients with possible DLB. For this purpose, blood is collected in PAXgene blood RNA tubes. After RNA purification and reverse transcription, relative expression levels are determined by real-time PCR. Diminished levels of at least two of the transcripts will be indicative for DLB, allowing its correct diagnosis.

"Biomarker 2" consists of the determination of 6 polymorphic sites within the regulatory region of another gene (gene B). A defined genotype combination will be consistent with the diagnosis of those DLB patients who show diminished levels of certain protein in the brain.

Diminished levels of "Biomarker 1" may reflect increased protein aggregation rates in the brain that represent a characteristic feature for the very first stages of Lewy body disorders. Signalling to the periphery (e.g. through miRNAs) may result in the diminution of gene A transcripts in blood. By substrate exhaustion at later disease stages, protein aggregation rate slows down cancelling the signalling and normalizing mRNA expression levels.

About 40% of DLB patient develop disease as a result of diminished levels of certain protein in the brain. We have identified six polymorphic sites as "Biomarker 2" within the regulatory region of gene B, responsible for this diminution. Future treatments directed to the increase those protein levels in the brain can be applied for the patients carrying those alleles or genotypes responsible for that phenotype.

TARGET INDICATIONS

Dementia with Lewy bodies (DLB), the second most frequent cause of dementia after Alzheimer disease (AD), is very aggressive with an overall survival of 6 years.

CURRENT STATUS

- The workflow established for the identification of diagnostic biomarkers in our lab includes three steps: (1) genomic and transcriptomic analysis of post-mortem brain samples and identification of possible markers, (2) analysis of a clinical cohort and validation of possible markers from step 1, (3) analysis of a multicenter clinical cohort and further validation of the marker.
- "Biomarker 1" has successfully finished step 2 validation.
- "Biomarker 2" has been identified in post-mortem brain samples being necessary its validation in steps 2 and 3.

INNOVATIVE ASPECTS

- Due to overlapping features between DLB and AD, the clinical diagnosis of DLB is still very difficult to achieve and the use of complementary diagnostic tools such as neuroimaging techniques are too expensive for their routine use.
- We have developed two different biomarkers for the early and differential diagnosis of DLB that will avoid misdiagnosis.
- So far, genetic biomarkers suitable as diagnostic tools for DLB have not been identified.

IPR

Two European patents were submitted this year 2015.

PARTNERING OPPORTUNITIES

We are looking for partnership to achieve final development including validation in step 3 for "Biomarker 1", and validation in steps 2 and 3 for "Biomarker 2" and/or for licensing out the biomarkers.

BIONURE

PROFILE

bionure
Promoting Neuroprotection

Bionure is a biotechnology company developing novel therapies for the treatment of rare, ophthalmological diseases. We are focused in acute optic neuritis (AON) and neuromyelitis optica (NMO), two inflammatory-mediated diseases closely related with Multiple Sclerosis that lead to visual impairment, blindness and paralysis. Bionure's main candidate is BN201, a NCE, first-in-class small molecule that promotes neuroprotection and remyelination and has obtained clearance from the Netherlands Agency to start Phase 1 studies. BN201 has also been granted orphan designation by FDA and EMA for AON. The company is led by Albert G. Zamora, CEO, and Pablo Villoslada, CSO.

SPEAKER

Gerard Caelles is a biotechnologist by background. Business Development Manager at Bionure for 4 years, mainly leading the fundraising and BD & Licensing efforts, dealing with pharmaceutical companies and venture capitalists.

gcaelles@bionure.com

PRODUCT

BN 201: 2nd generation program for acute optic neuritis (AON) and neuromyelitis optica (NMO)

MECHANISM OF ACTION

BN201 is a small molecule, new chemical entity, first-in-class SGK agonist that has completed regulatory preclinical studies and has obtained clearance from the Netherlands Agency to start a phase 1 study.

BN201 is an agonist of SGK2, an intracellular serine/threonine kinase that promotes cell protection and is activated in response to trophic factor signaling and stress (glucose, pH, ions, oxidative stress). Activation of SGK2 by BN201 leads to translocation of FOXO3 from the nucleus to the cytoplasm, promoting the expression of anti-oxidant and anti-apoptotic genes and inhibiting the expression of pro-apoptotic genes. SGK2 is widely expressed in all the neurons of the CNS. We have found that SGK2 is expressed in the brain of MS patients with long-term MS and its expression is increased in glial cells within the MS plaques.

BN201 has been shown to promote neuroprotection and remyelination in several animal models of inflammation, demyelination and neurodegeneration (Experimental Autoimmune Encephalomyelitis model, Lysolecithin-induced demyelination model and glaucoma hypertensive model, respectively).

TARGET INDICATIONS

Two orphan ophthalmological diseases: acute optic neuritis (AON) and neuromyelitis optica (NMO), chosen according to the properties of the candidate and the more feasible regulatory and clinical pathway.

CURRENT STATUS

- GLP toxicology performed with the clearance from the Netherlands Agency to conduct phase 1 study. DP Formulation and CMC in place.
- Preclinical POC well-established in several animal models of damage.
- Orphan designation by FDA and EMA for optic neuritis.
- Composition of matter patent granted in US, Europe and China and ongoing in the rest of countries.
- Clinical team in place in the US – former Genentech Neuro-ophthalmology clinical team
- Bionure's Phase 2 in AON will be completed by 2017 and early entry into the market is expected after a Phase 2/3 in the ultra-rare, severe and life-threatening disease NMO.
- In parallel with the phase 1, Bionure will run a 2nd generation program with the aim of developing new compounds with enhanced properties and new formulations for additional indications.
- AON is considered a unique clinical model for evaluating treatment response in the course of demyelination, axonal injury and neuronal degeneration; thus, after obtaining a clinical POC in AON (2017), we will pursue extension to the massive Multiple Sclerosis market as well as other neurodegenerative diseases.

INNOVATIVE ASPECTS

- AON develops as an acute, recurrent disease and is treated with intravenous corticosteroids for 5 days. Steroids do not have any effect on the visual outcome (symptomatic treatment) and there is a need for therapies preventing axonal damage and demyelination to improve the visual outcome and associated quality of life of patients. The most advanced compound in the pipeline is Biogen's BIIB033 (anti-lingo), a mAb that promotes remyelination and is currently in Phase 2 trials. Other competitors are Acorda's rHIgM22, another mAb promoting remyelination in Phase 1, and some academic-sponsored repurposing drugs in clinical trials such as EPO and Phenytoin for neuroprotection and Clemastine for remyelination.
- In the case of NMO, prophylactic, off-label immunosuppressive treatment (ie rituximab) is given to prevent relapses and when a relapse occurs, patients are treated with IV corticosteroids for 5 days. Clinical pipeline is based only on immunosuppressive drugs aimed at preventing relapses (Alexion's Eculizumab in Phase 3, MedImmune's MEDI-551 in Phase 2/3 or Chugai's SA237 in Phase 3) and there are no developments focused at treating relapses to prevent disability (paralysis, blindness).
- Overall, BN201 is the only candidate promoting neuroprotection and remyelination. We believe this is crucial, as promoting only remyelination (the process through which myelin wraps up axons, as the most advanced candidates BIIB033 or rHIgM22 do) may be futile if axons are not preserved.

IPR

Composition of matter patent granted in US, Europe and China and ongoing in the rest of countries. Freedom to Operate analysis performed by attorneys in US.

PARTNERING OPPORTUNITIES

Open to a licensing, co-development, option agreement or M&A, as well as to equity investment for the BN201 project as well as the 2nd generation program.

Pronacera Therapeutics

PROFILE

Pronacera Therapeutics is focused on rare diseases. Our expertise is in mitochondrial diseases, lysosomes diseases and autoimmune disorders. In fact, the current pipeline of Pronacera has two products in develop: (I) a pharmacological chaperone for Morquio/GM1 lysosome disease and (II) methods to stabilize apoptosis cells; several applications such as treatment of autoimmune diseases. We complete these lines with a business strategy that consists in "unusual" clinical analysis focused on requirements of patients with rare diseases.

SPEAKER

David Cotán, PhD, born in 1985 in Seville where obtained the graduate in Environmental science by Pablo de Olavide University. His career has been developed in research, mainly in rare diseases area, in fact, his doctorate (2010) discussed about this issue. Cotán has increased his experience in the business sector in companies such as Bionaturis (recombinant protein factory) and SINAE (scientific consulting). Nowadays, he combines his work in Pronacera

d.cotan@pronacera.com

PRODUCT

PRON01, pharmacological chaperone as treatment to GM1 and Morquio B lysosomal diseases

MECHANISM OF ACTION

A pharmacological chaperone is an innovative drug consisting of small molecules able to reach the CNS and act through stabilization of unstable proteins. Mutations in β-Gal cause a decrease in protein stability, which is degraded by the quality control system of the cell.

The absence of functional protein is the main cause of these diseases and the CFs help recovering such functionality and its transport to the lysosome, thus preventing further development of the disease.

PRON01 is a pharmacological chaperone indicated to recovery the β-Gal activity of mutated enzymes. There is a broad spectrum mutations in this protein that causes different phenotypes depending on CNS implication.

PRON01 is able to cross the blood brain barrier through an oral administration without delivery restrictions. This CF is an innovative therapy safe due to high affinity of the molecule for β-Gal enzymes, furthermore, no toxicity to high concentrations has been observed.

TARGET INDICATIONS

GM1/Morquio B lysosomal storage disorders belong to a group of rare diseases, low prevalence, resulting from abnormal metabolism of several substrates which are not degraded and accumulate in lysosomes. Currently there are only symptomatic therapies

available for these patients, differing therapeutic approaches: the substrate reduction therapy based inhibiting production substrate using inhibitors of enzymes involved in their biosynthesis, and enzyme replacement therapy (ERT), based on exogenous administration of recombinant active enzymes without effectiveness due to impossibility to cross blood brain barrier.

CURRENT STATUS

To date, PRON01 has completed activities in non-regulatory preclinical phase. In-vitro and in-vivo assays were performed in order to determine the affinity/selectivity for β-Gal enzyme, recovering lysosomal activity in human fibroblast derived from patients. Screening of chaperone effects on recombinant human β-Gal mutants showed response up to 24 over 88 mutant types.

The chaperone was orally administrated to experimental model mice expressing specific β-Gal mutation; a medically significant effect in the CNS at concentrations above 5 mM was observed. This implies that the drug passes through the membrane and gastrointenstinal blood-brain barrier.

INNOVATIVE ASPECTS

Actually there is not any similar product to treat these diseases. However, PRON01 has some key features that increase its value as potential drug. PRON01 has:

(I) high affinity and selectivity for β-Gal,

(II) it increases its stability against degradation.

(III) Oral administration and

(IV) the ability to cross the blood brain barrier are key differentiators to effectiveness of the development.

(V) The successful recovery for broad spectrum mutations (24/88) justifies their market value. Furthermore

(VI) it has been determinate no toxicity to high concentrations (up to 640 μM). Low costs of a production easily scalable.

IPR

Production and application of PRON01 is protected under number patent P201232024. We have the know-how and have presented new patent application where we claim the combinated administration with other molecule.

PARTNERING OPPORTUNITIES

Currently, the company is seeking partners to finalize the pre-clinical phase and continue the development of the lysosomal pharmacological chaperone under a cooperative model of co-development or returnable investment.