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

Décimo Encuentro de Cooperación Farma-Biotec
Enfermedades autoinmunes y cardiovascular

Miércoles, 27 de noviembre de 2013

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 siete propuestas para que realicen su presentación en la jornada del miércoles día 27 de noviembre en Madrid.

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.

Agenda prevista

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

09:15 09:30	Recepción, contactos informales, café	Estado de Desarrollo	Ponente
09:30 09:45	Bienvenida y presentación de la jornada		Farmaindustria
09:45 10:15	Uso de VIP como marcador pronóstico de enfermedades autoinmunes	Validado en pacientes del H.U. La Princesa	Isidoro González, H. U. LA PRINCESA
10:15 10:45	NT-KO-003, molécula de síntesis para el tratamiento eficaz de la Esclerosis Múltiple	Completada Fase Clínica IIa	Clara Campas, ADVANCELL
10:45 11:15	Biomolécula aplicada a inmunomodulación administrada como fármaco y mediante terapia celular.	Prueba de concepto en sistemas vivos	José Mª Arán. IDIBELL
11:15 11:45	Café, refrescos, contactos directos		
11:45 12:15	Biomarcador para fallo cardíaco, basado en la medida de una proteína específica soluble en suero sanguíneo.	Validado en 192 pacientes	Montserrat Batlle, H. CLINIC DE BARCELONA
12:15 12:45	Test para diagnosis temprana de la artritis reumatoide basado en péptidos quiméricos de fibrina y vimentina	Validado en más de mil pacientes	Isabel Haro, IQAC-CSIC
12:45 13:15	Nuevos derivados de nitronas con actividad antioxidante y neuroprotectora para el tratamiento del ictus y la isquemia cerebral	Probados en sistemas vivos	Alberto Alcázar, H. RAMÓN Y CAJAL
13:15 13:45	NmC, nueva molécula con potencial de eficacia y seguridad como antitrombótico y anticoagulante	Prueba de concepto en sistemas vivos	Jordi Naval ENEMCE PHARMA
13:45 14:30	Cierre, contactos directos, vino y tapas		

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: **Sede de Farmaindustria en Madrid. Calle María de Molina nº 54. 7ª pta.**
Fecha: **Miércoles día 27 de noviembre de 2013**

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

HOSPITAL UNIVERSITARIO DE LA PRINCESA

PROFILE

The Rheumatology Service of the HU La Princesa implemented in 2000 an early arthritis register that has allowed studying pathogenic mechanisms and different biomarkers. Several other registers of patients with autoimmune disorders are currently ongoing. On the other hand, The Department of Cellular Biology at Madrid U. Complutense (*Prof. Rosa P. Gomariz*) has a wide experience studying the effects of VIP on the immunological system both "in vitro" and in murine autoimmune models.

SPEAKER

Dr Isidoro González Álvaro is Coordinator of Advanced Therapies and Individualized Medicine at the Institute for Health Research "Hospital Universitario de La Princesa". He has wrote more than 70 articles in Pubmed. PI of 6 public research projects funded by Instituto de Salud Carlos III since 1998 up to now, all of them focused on pathogenic mechanisms in rheumatoid arthritis and development of prognostic biomarkers in early arthritis.

isidoro.ga@ser.es

PRODUCT

VIP serum levels as prognostic biomarker in patients with rheumatoid arthritis

MECHANISM OF ACTION

VIP has been involved in the differentiation of Th lymphocytes decreasing the production of proinflammatory mediators and administration of exogenous VIP ameliorates arthritis in murine models. It is likely that those patients who are unable to up-regulate their VIP levels when they develop RA, show a worse clinical course.

TARGET INDICATIONS

The product is under the scope of inflammatory and autoimmune disorders. The usefulness of this product is selecting patients that would be candidates to a more intense treatment, probably including biologic therapy as first line.

CURRENT STATUS

- A population of 91 patients with early arthritis has been studied.
- Those RA patients with VIP levels below the 25th percentile of the normal population are those with poor prognosis. The outcomes that have been studied are the level of disease

activity as well as the cumulative treatment after 2 years of follow-up.

- In addition, it has been observed that having low VIP levels is a finding that does not change along the follow-up of the patient. This represent an advantage since its prognostic value is independent of treatment prescribed or the stage of the disease.
- Frozen storage of serum samples does not interfere with the detection of VIP levels.
- The effect of low VIP levels in radiological progression is currently under study

INNOVATIVE ASPECTS

Rheumatoid arthritis (RA) and other autoimmune disorders can lead to severe disability and increased mortality. Early intensive immunomodulatory treatment is the best approach to slow progression and change long-term outcome.

However, it is important to detect those patients who are destined to have a more benign disease to avoid over-treating them. Probably the only validated prognostic factor in RA is anti-citrullinated protein antibodies (ACPA). There are no validated biomarkers for other autoimmune disorders.

Having low VIP serum levels is a biomarker of worse clinical course and higher requirements of treatment in patients with early arthritis.

The relevance of this new biomarker is that it improves the predictive value of ACPA since detect ACPA negative patients at risk of poor evolution and those with both biomarkers exhibited higher requirements of treatment.

IPR

At present the product has been protected at local level through the patent P201230827 "Use of VIP as prognostic marker in autoimmune diseases". The PCT phase has been initiated.

PARTNERING OPPORTUNITIES

Pharmaceutical companies have greater convening power in order to validate our findings and therefore to increase the commercial interest of the product.

Those pharmaceutical companies with diagnostic section would be the most interested on this product, especially if the company has an ACPA detection kit among its products. In this case, providing kits with the capability to detect both low VIP levels and ACPA would be a competitive advantage in this market.

In addition, pharmaceutical companies with biological therapies already marketed may benefit of detecting low VIP levels, since these patients may be candidates for these types of treatments. This is especially interesting in the case of TNF blocker, since we have observed that these drugs may increase VIP levels.

ADVANCELL-NEUROTEC

PROFILE

ADVANCELL, S.A. is a privately owned biopharmaceutical company that generates drug candidates by acquiring rights from public and private research centers and develops these products to clinical proof of concept (Phase 2). Advancell currently has 3 programs in clinical investigation in the fields of Oncology and Neurology and aims to partner these programs with pharmaceutical companies to complete development to market and commercialize the products worldwide.

NEUROTEC PHARMA, S.L. is a biopharmaceutical company, privately owned, focused on the development of new treatments for Central Nervous System diseases with neuroprotective and anti-inflammatory effects. Neurotec works with accepted animal models of CNS diseases and its business model is based on reprofiling of drugs for their development in CNS diseases from its Preclinical Phase up to Clinical Phase I-II with the aim to increase their value and transfer them to third parties by out licensing.

SPEAKER

Dra. Clara Campàs-Moya, is Managing Director of the biopharmaceutical company ADVANCELL and co-author of the patent Acadesine, the first drug originated in a Spanish public University that successfully reached clinical trials. Dr. Campàs-Moya is member of the scientific committee of the venture capital fund HealthEquity, member of the Steering Committee at CataloniaBIO and member of the board of trustees of Biocat. She holds a PhD in Pharmacy by Universitat de Barcelona and has extensively published in scientific journals.

clara.c@advancell.net

PRODUCT

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

MECHANISM OF ACTION

NT-KO-003 target is a defined KATP channel expressed in several cell types. NT-KO-003 exerts a direct neuroprotective effect in neurons, has a CNS anti-inflammatory effect (glial mediated) and has shown to have anti-demyelinating properties. The ability of the drug to induce remyelination is being investigated.

TARGET INDICATIONS

The main indication of NT-KO-003 is treatment of MS. A potential additional indication under evaluation is Amyotrophic Lateral Sclerosis (ALS).

CURRENT STATUS

- NT-KO-003 has shown efficacy in accepted MS animal models (non-clinical proof of concept). The drug has shown to be safe and well tolerated when administered orally to MS patients chronically (NeuroAdvan Phase 2a study, Europe). Efficacy results of the Phase 2a trial conducted will be presented during the JP Morgan Conference (San Francisco, January 2014)

INNOVATIVE ASPECTS

- NT-KO-003 is a small molecule under clinical development for the Treatment of Multiple Sclerosis (MS).
- The drug is administered orally, once a day, in film coated tablets.
- NT-KO-003 has shown efficacy in several non-clinical MS experimental approaches.
- Its novel mechanism of action (neuroprotection, CNS-anti-inflammatory and anti-demyelination effects) differs from classical MS drugs. The drug does not induce immunosuppression and its good safety profile makes it a good candidate for combination to other drugs.
- The drug has shown to be safe and well tolerated when administered chronically to patients suffering MS. Efficacy results of a Phase 2a study conducted in Europe will be presented in January 2014.
- Oral administration and its tolerability are key competitive advantages of NT-KO-003 when compared to current drugs in MS. These are 2 key factors to achieve patient's adhesion to treatment in this chronic condition affecting young adult populations.

IPR

Two PCT applications (patents of use) are requested worldwide.

PARTNERING OPPORTUNITIES

Advancell and Neurotec aim to partner the program after Phase 2a. Partner will assume lead role in development to market and will commercialize the product. We seek a customary licensing transaction - upfront, milestones and royalty. Global rights available (November 20013).

IDIBELL

PROFILE

IDIBELL is a research centre focused on cellular medicine, where the high level basic research is devoted to unravel relevant clinical questions and to foster the economic development.

The **"Immune-inflammatory Processes and Gene Therapeutics"** team, headed by Dr. Aran, is a dynamic group integrated in the Molecular Genetics Laboratory, with specific training in the areas of human genetics, biochemistry, and molecular and cell biology, interested in translational biomedical research and focused to the study of the molecular basis of the immune-inflammatory processes.

SPEAKER

Dr. Josep M. Aran has a wide experience in the areas of molecular and cell biology, gene transfer and therapy, gained during a six year stay in USA scientific Institutions. Nowadays he is a senior researcher and Group Leader in the Molecular Genetics Laboratory (IDIBELL). He has worked extensively uncovering the molecular basis of the immune-inflammatory processes, and developing novel gene and cell therapy strategies to mitigate immune-inflammatory pathology in several animal models. He has been awarded with 12 translational research Projects as Principal Investigator, published 50 research papers in leading biomedical journals, authored several book chapters and journal reviews, holds 5 international patents, and has been supervisor of 6 PhD students.

jaran@idibell.cat

PRODUCT

C4BP(β–): a therapeutic anti-inflammatory and immune-modulatory agent in autoimmunity

MECHANISM OF ACTION

A healthy immune system recognizes and eliminates invading pathogens, but preserves tolerance for self-antigens. In contrast, autoimmune diseases develop when self-antigens are recognized as foreign by the immune system, resulting in hyperactivity of both cellular and humoral immunity against these antigens. Dendritic cells play a central role in maintaining the balance between (auto)immunity and tolerance. Hence, there is a strong need for agents or methods that generate properly equipped DC that can efficiently induce antigen-specific immune tolerance.

The composition is based on the isoform of the complement C4BP lacking the β chain, which is capable of inducing a tolerogenic state in dendritic cells, and to the uses thereof for the prevention and/or treatment of diseases characterized by a un undesired activation of the immune system.

TARGET INDICATIONS

Autoimmune diseases (systemic lupus erythematosus (SLE), diabetes mellitus, asthma, ulcerative cholitis, Grave's disease, arthritis, including rheumatoid arthritis and osteoarthritis, pernicious anemia, and multiple sclerosis, among numerous others)

Transplantation (transplant rejection, ischemia-reperfusion injury, GvHD,…)

CURRENT STATUS

- It has been shown that the complement regulator C4BP minor isoform, C4BP(β-), is able to induce a semi-mature, tolerogenic state in dendritic cells when activated by a pro-inflammatory stimulus. These cells are characterized by specific traits: morphologic (resembling immature dendritic cells), phenotypic (low co-stimulatory molecules expression, inability to release pro-inflammatory Th1-cytokines (IL-12, TNF-a, IFN-g, IL-6, IL-8) and increased secretion of anti-inflammatory IL-10,…) and functional (inability to induce allogeneic T cell proliferation, capability for Treg generation,…).
- Proof-of-concept pre-clinical study of the in vivo efficacy of C4BP(β-) in a humanized mouse model of graft-versus-host disease (GvHD).

INNOVATIVE ASPECTS

- Novel anti-inflammatory and immune-modulatory physiological C4BP(β-)-based therapy.
- Efficacy of naturally occurring C4BP(β-) without the side effects of the present immunosuppressive and anti-inflammatory drugs.
- To perform pharmacological therapy (direct C4BP(β-) administration), or cell therapy using ex vivo C4BP(β-)-conditioned dendritic cells.
- Synergistic potential of use together with other conventional drugs.

IPR

Patent title: "Compositions and methods for immunomodulation" European patent application: EP11382240 (15/07/2011) PCT/EP2012/063932 (16/07/2012)

PARTNERING OPPORTUNITIES

Usually through licensing agreements, but also through funding R & D collaborative projects related with different aspects of the invention (pre-clinical and clinical co-development…).

HOSPITAL CLINIC DE BARCELONA

PROFILE

The **Heart Failure and Heart Transplantation** (HFHT) research group has more than 15 years of experience in research and is composed by a group of highly specialized cardiologists from the Cardiology Department at **Hospital Clinic of Barcelona** and by basic researchers. The present project started as a joint effort with the group of Dr. García de Frutos at **IIBB-CSIC**, an expert on vitamin K-dependent proteins and their receptors in the fields of hemostasis and human pathology.

SPEAKER

Dra. Montserrat Batlle Perales is a Researcher in Cardiology at the Institut d´Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS) and at the Cardiology Department at the Institut Clínic del Tòrax, Hospital Clínic de Barcelona. Ph.D. in Biomedical Sciences. Mount Sinai Hospital-New York University, New York.

mbatlle@clinic.ub.es

PRODUCT

Soluble protein AXL as a Heart Failure biomarker

MECHANISM OF ACTION

The sAXL peptide is the product of ADAM protease action on the membrane receptor tyrosine kinase AXL. AXL is a member of a vertebrate-specific family of receptor tyrosine kinase widely expressed in human tissues, but with a high level of expression on cardiomyocytes. Its role in tissue homeostasis is related to mechanisms of response to damage, including tissue response to inflammation, innate immunity and tissue repair. The main ligand of this receptor is the vitamin K-dependent protein GAS6.

TARGET INDICATIONS

The biomarker sAXL is useful in chronic and stable HF prognosis adding predictive value to BNP. Further research is needed in order to ascertain if it could be useful to diagnose HF in the acute setting and to help discriminate between HF patients and patients with other pathologies

CURRENT STATUS

- It has been demonstrated that sAXL serum values are higher in heart failure patients than in controls and that it can be a good HF prognostic biomarker complementary to BNP. Specificity of sAXL as a HF biomarker has been studied analyzing patients with other cardiovascular and respiratory pathologies.
- It has been detected 6-fold higher AXL protein levels in hearts from HF patients that underwent cardiac transplantation, supporting the putative cardiac origin of the peptide in serum.

INNOVATIVE ASPECTS

- sAXL in serum is increased in heart failure (HF) patients with reduced ejection fraction (HF-REF, n=192) when compared to controls (n=67, P<0.0001).
- Furthermore, sAXL levels correlated with numerous parameters associated with worse HF prognosis but not with echocardiographic parameters.
- Therefore, its behavior differs from brain natriuretic peptides (BNPs), the "gold standard" biomarkers of HF.
- Cox regression analysis indicated that high sAXL values at enrollment time were related to the major HF events (all-cause mortality, heart transplantation and HF hospitalizations) at one year follow-up (P<0.001), adding predictive value to high BNP levels.
- Preliminary results with other groups of patients sustains the role of sAXL in HF, as we also find higher sAXL values in HF patients with preserved ejection fraction (HF-PEF) and we do not find higher values in patients suffering from other cardiovascular pathologies such as acute myocardial infarction or atrial fibrillation.

IPR

On August 2013 our patent with the title: Use of the soluble form of AXL in the diagnosis and/or prognosis of Heart Failure Syndrome was published with the International Publication Number WO 2013/120830 A1. The Extended European Search Report (P2159EF00) considered that the patent complied with the conditions of novelty and industrial application.

PARTNERING OPPORTUNITIES

We are interested in partners who would include sAXL as a prognostic biomarker. We are interested in developing a flexible and automatized measurement protocol with the latest technologies applied to diagnosis

CSIC

PROFILE

The Unit of **Synthesis and Biomedical Applications of Peptides** led by Dra. Isabel Haro has been working with peptides for over 25 years. Currently the group is researching on peptide chemistry from three different perspectives: design (lipoderivatives, cyclic, multimeric peptides, coordinated with gold), synthesis (solid phase and solution) and research into their possible applications, both in therapy (HIV entry inhibitors, peptide controlled-release nanosystems for ocular administration of drugs) and in the diagnosis of human diseases (rheumatoid arthritis, HIV/GBV-C co-infection).

SPEAKER

Dra. Isabel Haro gained a permanent position in the CSIC in 1990 after a post-doctoral training of two years between the CSIC in Barcelona and the Royal Free Hospital in London. Since then she has been working in the use of synthetic peptides in the field of Biomedicine and has published more than 180 articles, 8 reviews, 30 chapters of books and 8 patents. Also, she has been the principal researcher of 15 research projects and 3 contracts with the industry and supervised 12 doctoral theses. Currently, she is also member of the coordination group of Chemical Science and Technologies in CSIC.

isabel.haro@iqac.csic.es

PRODUCT

Early diagnosis and prognosis of rheumatoid arthritis based on citrullinated peptides.

MECHANISM OF ACTION

Antibodies to citrullinated (arginine is replaced by a citrulline) proteins/peptides (ACPAs) are the most specific serological markers for diagnosing RA. We have developed an ELISA assay based on chimeric citrullinated synthetic peptides derived from fibrin, filaggrin and vimentin protein as antigenic substrates.

TARGET INDICATIONS

Antibodies to citrullinated chimeric peptides can be good markers in patients suffering from Rheumatoid Arthritis, especially those showing poor radiographic outcome and that need more aggressive therapy from the beginning of the diagnostic. They are very useful in combination to improve the sensitivity in the identification of particular subsets of RA patients.

CURRENT STATUS

The chimeric citrullinated peptides-based ELISA test has been tested with more than 900 sera (332 patients with RA, 113 with psoriatic arthritis, 119 with systemic lupus erythematosus, 84 with hepatitis C infection and 307 blood donors) to control the sensitivity and specificity and compared with the commercial CCP2-based test in a stratified study.

Autoantibodies (ACPAs) were also analysed at baseline and during a 2-year follow-up in 98 early RA patients to determine their prognostic value. The obtained results highlight that our test is highly sensitive and specific for RA and is able to detect ACPAs in RA patients when

other commercial tests failed. Moreover, early RA patients with anti-chimerics antibodies, including those who are CCP2 negative, show greater radiographic progression.

INNOVATIVE ASPECTS

- Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes joint inflammation and extra-articular manifestations affecting 1% of the world population. To prevent progressive and irreversible structural damage, early diagnosis of RA is of paramount importance. Antibodies directed against citrullinated proteins and peptides (ACPAs) are the most specific serological markers available for diagnosing RA.
- We have developed the application of chimeric peptides bearing different citrullinated protein domains for the design of RA diagnosis systems. These peptides have a high sensitivity and specificity for RA and are able to detect ACPAs in RA patients who are false negatives with commercial tests and also give better results in terms of identifying patients with poor radiographic outcome.

IPR

Priority date: 28/07/2011 International PCT extension (PCT/ES2012/070555). Published as WO2013014312. Applicants: *Consejo Superior de Investigacions Científicas* (CSIC) and *Fundació Clínic per a la Recerca Biomedica* (FCRB)

PARTNERING OPPORTUNITIES

CSIC and FCRB are seeking for out-licensing the technology to pharmaceutical and/or diagnostic companies in order to final development and commercialization of an RA diagnosis kit.

HOSPITAL RAMÓN Y CAJAL

PROFILE

The research Group led by Dr. Alcazar investigates the mechanisms of death and neuroprotection in cerebral ischemia. He has worked largely in the translation inhibition control, which plays a key role in ischemic pathology. The Group use in vivo experimental models of transient cerebral ischemia (global and focal) and primary neuronal cultures subjected to ischemia in vitro. In these models, he has tested new drugs with potential use against cerebral ischemia

SPEAKER

Dr. Alberto Alcazar Gonzalez is a PhD in Biology by the Universidad Complutense de Madrid, and Master in Molecular Biology by the Universidad Autónoma de Madrid. Researcher of the Dept. of Investigation, in the Hospital Ramón y Cajal-IRYCIS, Madrid, and Leader of the Neuroproteins and Ischemia Laboratory.

alberto.alcazar@hrc.es

PRODUCT

Quinoline and steroidal nitrones with neuroprotective activity for the treatment of ictus

MECHANISM OF ACTION

The nitrone group acts as a radical scavenger and reduces oxidative stress.

Known nitrones like phenyl-t-butyl nitrone (PBN) and NXY-059, had shown a high activity as antioxidant agents, however, their in vivo efficacy is limited, probably due to low cell permeability.

Taking into account the excellent antioxidant characteristics of nitrone compounds, the search of new derivatives with major activity and better permeability is of great interest in the area of neurodegenerative diseases.

TARGET INDICATIONS

The use of nitrone derivatives represents a promising therapeutic alternative approach for the treatment of diseases like Ictus and other neurodegenerative diseases, as Alzheimer, Parkinson and Amyotrophic Lateral Sclerosis (ALS), acting as radical scavengers and reducing oxidative stress common in all these diseases.

CURRENT STATUS

- These compounds have shown a high neuroprotective effect on primary neuronal cell cultures exposed to oxygen-glucose deprivation (76.9 % of neuroprotection at 50 □M, and 80.7% of neuroprotection at 5 μM for quinoline and steroidal nitrones, respectively)
- In vivo assays in global cerebral ischemia animal models show that these compounds are able to significantly decrease neuronal dead.
- All the compounds are easily prepared from commercially available starting materials in a rapid process with good chemistry yield.

INNOVATIVE ASPECTS

- The use of nitrone derivates represents a new and interesting approach for the treatment of diseases like ictus or ischemia, related with the oxidative stress-induced injury after reoxigenation.
- The presence of a quinoline group in the structure of the molecules increases their lipophilicity and can improve their cell permeability.
- In addition, it is well known the neuroprotector capacity of steroids, specifically in inflammatory processes affecting the central nervous system (CNS).
- In vitro assays in cell cultures show that these compounds have high neuroprotective activity against ischemia-reoxigenation in vitro.
- Furthermore, the compounds are able to cross the blood-brain barrier, which, together with their antioxidant activity, make them especially useful as drugs for the treatment of CNS diseases

IPR

Quinoline nitrones: Pat nº P201131338 from 01/08/2011; PCT from 24/07/2012

Steroidal nitrones: Pat nº P201330738 from 22/05/2013

PARTNERING OPPORTUNITIES

Financial support for performing a large scale proof of concept in global and focal cerebral ischemia animal models. Application to public financial supports like INNPACTO

ENEMCE PHARMA

PROFILE

Enemce Pharma

The goal of ENEMCE PHARMA SL is to develop new drugs for cardiovascular diseases as new chemical entities based on new SSRI derivatives. Enemce holds global license of patents covering new chemical derivatives from SSRIS (citalopram, fluoxetine, and others) that have shown promising antithrombotic effects, with fewer adverse events, and by a completely new mechanism of action. The company has expert management and its operations are based in manufacturing and testing outsourced to reputable contract research organizations, and critical responsibilities assumed by dedicated independent individuals. The company has offices in Barcelona and Quebec.

SPEAKER

Dr. Jordi Naval, Chief Operations Officer. With more than 18 years of experience in the bio-pharmaceutical industry. he founded the CRO Infociencia in 1997, that reached 120 employees and 8 m in revenues in 2008, when the company was sold to Research Pharmaceutical Services. Dr. Jordi naval co-founded Anaxomics, a drug discovery company based on biocomputational approaches, where he was CEO until July 2013.

navalj@lifscie.com

PRODUCT

NMC, a new antithrombotic candidate aimed to a multibilion dollar market

MECHANISM OF ACTION

Serotonin is a potent activator of platelets in thrombus formation. Serotonin is uptaked from plasma and stored in internal granules within the platelets. The Serotonin reuptake transporter (SERT) channel protein is similar to the one found in neurons, and Selective Serotonin Reuptake Inhibitors (SSRIS) are also inhibitors of SERT in platelets.

The new chemical derivative of Citalopram, a widely used SSRI, called NMC, is an inhibitor of SERT in platelets, and because it is positively charged, it does not cross Blood-Brain Barrier.

Our hypothesis is that NMC reduces the uptake of Serotonin in platelets, reducing the adhesion/activation/aggregation potential of platelets in blood, with a clear antithrombotic effect.

We have positive results in vitro and in animals showing the antiplatelet effect of NMC..

TARGET INDICATIONS

Main indication is an antithrombotic of general use. Strategy could be to be used initially for Atrial Fibrilation, and afterwards expand to other markets.

CURRENT STATUS

- Initial stages have been covered for proving efficacy and safety in non-GMP preclinical experiments- The PK parameters of NMC have also been studied.
- A method for producing NMC has been stablished
- NMC has same affinity for SERT than Citalopram (in vitro)
- NMC does not cross BBB (mice)

- NMC does not have antidepressant effect (mice)
- NMC does not bind to hERG (in any case, less than Citalopram)
- We have conducted PK studies in rats with NMC and citalopram. Oral absortion is higher for Cit than for NMC. Other PK parameters are very similar, including DME.
- NMC inhibits Serotonin uptake by human platelets (in vitro)
- NMC inhibits human platelet aggregation in vitro, both induced by 5HT and by ADP, and shows synergistic effect with Aspirin.
- We are currently developing a formulation of NMC to improve oral absortion

INNOVATIVE ASPECTS

- NMC is the n-metil derivative of the well known SSRI Citalopram. Epidemiological studies with thousands of patients have shown that patients taking SSRIs as antidepressants show substantially less Myocardial Infarctions and Strokes.
- NMC is a quaternary ammonium derivative of citalopram that does not cross blood-brain barrier, and thus does not show antidepressant effects, while keeping systemic antiaggregation effects. Epidemological data also shows that SSRIS are safe, and do not produce bleeding in chronically treated patients.
- Thus, NMC is a promising antithrombotic candidate, with a new MoA, with similar efficacy and superior adverse events profile in respect to current products in the market (Plavix and aspirin)

IPR

World wide patent has been applied for covering composition of matter (new chemical entities): NOVEL SEROTONIN REUPTAKE INHIBITORS AS DRUGS HAVING PERIPHERAL-SYSTEM-RESTRICTED ACTIVITY (China, India, Germany, France, UK, Spain). The patent covers not only N-metil-citalopram, but a collection of other SSRI derivatives from fluoxetin, paroxetin, escitalopram, and others.

PARTNERING OPPORTUNITIES

As of today, we are looking for angel financing for improving oral bioavailability (100-150 k). If oral availability is improved over a certain threshold, we will initiate regulatory preclinical studies. At this stage, we will need (a) either 2-3 M eur for preclinical and CMC, or (b) partner with a pharma company for co-development of main candidate. In parallel we will screen and explore other candidates in the family of new systemic SSRIS. But we are open to other creative solutions.