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

XV Encuentro de Cooperación Farma-Biotech

Martes, 15 de noviembre de 2016

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 15 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.

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

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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:

Hora	Presentación	Estado de Desarrollo	Ponente
08:45 09:15	Recepción, contactos informales, café		
09:15 09:30	*Bienvenida y presentación de la jornada*		***Javier Urzay*** FARMAINDUSTRIA
09:30 10:00	*Ciclatop, fármaco para el tratamiento de la dermatitis atópica*	Fase Clínica II en curso	***Luis Ruiz Ávila*** SPHERIUM BIOMED
10:00 10:30	*BO112, Fármaco para el tratamiento de tumores sólidos*	Aprobada Fase Clínica I	***Marisol Quintero*** BIONCOTECH
10:30 11:00	*Inhibidores de CDK8*	Ensayos preclínicos	***Joaquín Pastor*** CNIO
11:00 11:30	*Agonistas B3 para el tratamiento de la hipertensión pulmonar*	Ensayos preclínicos	***Ana García Álvarez*** CNIC
11:30 12:00	Café, refrescos, contactos directos		
12:00 12:30	*miRNA mimic para tratar linfomas No Hodgkin*	Ensayos preclínicos	***Antonio Quesada*** CNIC
12:30 13:00	*Conjugado de metanfetamina y ácido oleico para tratamiento de la esteatohepatitis*	Ensayos preclínicos	***Fernando Rodríguez*** IBIMA
13:00 13:30	*Terapia no convencional con células madre*	Ensayos preclínicos	***Juan Muñoz*** FIBICO
13:30 14:00	*Nanoconjugado para el tratamiento del cáncer colorectal metastásico*	Ensayos preclínicos	***Ramón Mangues*** UAB - Hospital de Sant Pau
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: **Sede de Farmaindustria en Madrid. Calle María de Molina nº 54. 7ª planta**
Fecha: **Martes día 15 de noviembre de 2016**

La plataforma tecnológica Española Medicamentos Innovadores, cuenta con apoyo financiero del Ministerio de Economía y Competitividad (PTR-2016-0740)

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

SPHERIUM BIOMED

PROFILE

Spherium is a clinical stage company that sources its pipeline from academic research, with the ultimate goal of translating groundbreaking biomedical knowledge to the development value chain and the patients needs, through the following process:

1) Licensing innovation opportunities from universities &research institutions

2) Conducting the key activities and experiments to achieve a relevant value milestone

3) Finding the optimal partner to keep the project in track towards the market.

SPEAKER

Luis Ruiz Ávila, CEO of Spherium**,** is a molecular biologist by training, with experience in academic research, pharmaceutical drug development and biotech start-up creation and management.

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PRODUCT

Ciclatop

MECHANISM OF ACTION

Cyclosporine is a well-known and widely used immunosuppressant acting as a calcineurin inhibitor. The mechanism of action is validated for the target indications, since systemic cyclosporine is approved for its use in severe atopic dermatitis and psoriasis. The key aspect of the project is its formulation as topical product minimizing systemic exposure.

TARGET INDICATIONS

Dermatology: Mild And Moderate Atopic Dermatitis and Psoriasis.

Entry indication: Atopic Dermatitis.

CURRENT STATUS

- Preclinical data package completed, including local safety, systemic exposure, efficacy, skin penetration and pharmacodynamics.
- CMC development completed, including 12 months ongoing stability data and GMP scale (12kg batch)
- First clinical trial in atopic dermatitis approved by the Spanish agency, to start recruiting patients in September. The trial involves 8 centers in Spain and includes a paediatrics (2 to 12) and a juvenile (12 to 18) cohort.

INNOVATIVE ASPECTS

- It will be the first topical cyclosporine for dermal use.
- It can be the first one formulated as an spray.
- It has the potential (still to be demonstrated in clinical trials) to reduce pruritus and burning related to tacrolimus, the closer competitor.
- It could be adopted as the standard of care after corticorticoid therapy in paediatric population, a population less prone to receive systemic products.
- Since it is widely used in severe patients, with its use limited by its nephrotoxicity, having it available for the dermal route without systemic exposure is very attractive to dermatologist, in need for having further alternatives to the current topical options.

IPR

Broad and fresh patent coverage: general umbrella patent application from 2011 and selection patent for the specific family including cyclosporine from 2016.

PARTNERING OPPORTUNITIES

Looking for a development and commercial partner after clinical proof of concept..

BIONCOTECH

PROFILE

BiOncoTech Therapeutics is a biopharmaceutical company focused on the development of a new agent in immuno-oncology. The company was founded in 2010 as a spin-off of the Spanish National Cancer Research Center (CNIO), an institution that ranks among the world's leading cancer research centers. Bioncotech appointed four members of its SAB: Dr. Antoni Ribas, Dr. Manuel Hidalgo, Dr. Ignacio Melero and Dr. Holbrook Kohrt (until Feb 2016).

SPEAKER

Marisol Quintero, Managing Director, has great experience in Technology Transfer and Innovation in the oncology field. Prior to joining Bioncotech Dr. Quintero was Director of Innovation at the Spanish National Cancer Research Institute (CNIO) where she implemented mechanisms to translate promising new discoveries from the laboratory to the commercial development stage and to society in general. Dr Quintero holds an Executive MBA from IE Business School and a PhD in Pharmacology from University College, London.

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PRODUCT

Clinical candidate BO-112

MECHANISM OF ACTION

BO-112 is a nanomedicine that has been designed to target MDA5 a cytosolic helicase capable of stimulating innate and adaptative immune responses and triggering apoptosis in cancer cells. BO-112 overcomes nuclease degradation and cytosolic delivery by engulfing a specific chain of Poly I:C with a polycationic polymer.

BO-112 recapitulates the effect of viral infection activating cytosolic immune receptors for viral RNA species, and as such represents an attractive tool to enhance the therapeutic effect of immune therapies that act "releasing the brakes" of the immune system BO-112 constitutes a novel paradigm involving potent anti-tumoral mechanism with an innovative and sustained mode of action that promotes (i) selective induction of apoptosis and autophagy in tumor cells independent from the mutational status of classical oncogenes, such as BRAF, and (ii) systemic effects such as immune stimulation. Both local and systemic effect of BO-112 promotes a potent and selective tumor cell death. The anti-tumor activity of the BO-112 has been observed in a full battery of tumor cells in vitro and in different in vivo models.

TARGET INDICATIONS

BO-112 targets solid tumors. The FIH study target population includes patients with aggressive solid tumors from whom biopsies can be obtained.

CURRENT STATUS

- Bioncotech obtained the approval from the Spanish Regulatory agency to initiate clinical activities in May 2016. The FIH study for BO-112 is now active.

INNOVATIVE ASPECTS

- Demonstrated anti-tumor efficacy in vitro and in vivo cancer models.
- Efficacy independent of mutation status.
- Can be administered both systemically and intra-tumorally.
- Sinergistic effect when combined with other immuno-oncology agents.
- In vitro studies developed by Bioncotech prove that treatment of B16-F10 melanoma cells with BO-112 leads to a potent induction of mRNA IFN type I and an increase in PDL-1 expression. Furthermore, in vivo studies showed in mice injected sub-cutaneously with B16-F10 melanoma cells that the combination of intra-tumoral administration of BO-112 with anti-PDL1 more than doubled the survival time when compared to anti-PDL1 treatment alone.
- Combination with well-established agents brings alternative benefits by sensitizing tumor cells towards apoptosis and overcoming tumor-mediated immunosuppression. BO-112 can be delivered directly into the tumor, allowing much higher concentrations of the product in the tumor microenvironment than do systemic infusions, providing lower toxicity and better efficacy when combined with other agents.

IPR

Bioncotech licensed the technology own by CNIO and protected by the patent "PROCEDIMIENTO DE IDENTIFICACIÓN DE AGENTES TERAPÉUTICOS CONTRA EL MELANOMA Y USO DE AGENTE IDENTIFICADO" (P200930417). In 2015 the company submitted a new patent application to Project the pharmaceutical composition that describes the clinical candidate. ("NOVEL PHARMACEUTICAL COMPOSITION"EP15194864.3).

PARTNERING OPPORTUNITIES

We are interested in partnerships to explore the therapeutic opportunities of BO-112 in combination with other agents. We would like to establish collaborations for the development of combination studies in the immuno-oncology area.

CNIO

PROFILE

The CNIO ETP (*Experimental Therapeutics Programme*) functions as a bridge between discoveries in cancer biology at CNIO basic research labs and the pharma industry by applying the early phases of the drug discovery process, which allow the identification of advanced lead compounds with proven preclinical in vivo Proof of Concept (PoC) results as potential innovative anti-cancer therapies. Our team is constituted by biologists and medicinal chemists. We have capabilities to perform HTS, Hit Generation using rational design and the well known phases of HtL and LO including in vivo pharmacology. As a result of this model, several Drug Discovery projects have delivered advanced candidates with demonstrated in vivo PoC results and optimized profiles. Three classes of kinases inhibitors have already been licensed to Inflection Biosciences and Merck Serono for their clinical development. Currently we are working in several drug discovery projects in collaboration with CNIO researches and other international collaborators at VIB (Belgium). A brief introduction to our pipeline will be provided during the presentation

SPEAKER

Joaquin Pastor obtained his Ph.D. in Organic Chemistry at the University of Alcalá in 1994. He carried out his post-doc at the laboratory of Prof. K.C. Nicolaou at the Scripps Research Institute, USA. After almost 4 years, he joined Janssen as Head of High-throughput Medicinal Chemistry. He was Medicinal Chemistry Team Leader in several projects dedicated to CNS, Metabolic Disorders and Oncology drug discovery. Additionally, he was appointed as Head of the Hit Generation Team for CNS Europe. After 10 years he moved to CNIO as Director of Medicinal Chemistry in 2008. He was promoted in 2011 to his current role of Director of ETP. He has contributed to establish the operating model in which ETP functions as a bridge between discoveries in cancer biology at CNIO and the pharma industry to facilitate the discovery of innovative therapies in cancer. Dr. Pastor is co-author and inventor in 44 scientific publications and 36 patents in the field of drug discovery.

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PRODUCT

Novel orally available and selective CDK8 inhibitors

MECHANISM OF ACTION

We have generated the corresponding SAR/SPR data regarding primary activity, selectivity, in vitro ADMET and in vivo PK for a selected chemical series of CDK8 inhibitors. This information has been used for the identification of ETP-827 as our first selective orally bioavailable CDK8-i lead compound. ETP-827 has been profiled in in vivo PK-PD and efficacy studies in tumor models with preliminary positive results. Therefore, ETP-827 represents a first advanced lead CDK8-i emerging from our CNIO tricyclic chemical series and warrants further exploration of this series to obtain even more advanced and optimized compounds.

CDK8, a transcriptional kinase, activates □-catenin, a core regulator of canonical Wnt signaling in colon and gastric cancers. Moreover, CDK8 has been identified to be essential in cell proliferation in melanoma. The CDK8 gene is amplified in about 60% of colorectal cancers. CDK8 gene expression also correlates with a worse prognosis in colon, breast and

ovarian cancer. Recent reports support the potential of CDK8 inhibitors to treat Wnt dependent colorectal cancers using a CDK8-i in in vivo models. Additionally, CDK8 inhibition has demonstrated antileukemic activity in in vivo AML models through upregulation of Superenhancer-associated genes with tumor suppressor activity. Here, we present our novel CDK8-is as potential therapy to treat such type of cancers

TARGET INDICATIONS

The Mediator complex-associated kinase CDK8 and its closely related paralog CDK19 are transcription-regulating kinases. CDK8 has been shown to regulate several signaling pathways that are key regulators of cancer. As CDK8 is a regulator of the WNT/□-catenin signaling pathway, it may be associated with disorders and diseases where activation of the WNT/□-catenin pathway plays a role, among them hyperproliferative, inflammatory or degenerative disorders. A recent report also connects CDK8 inhibition with a potential treatment for obliterative vascular diseases arising from neointimal formation after vascular surgery.

CURRENT STATUS

- The CNIO´s CDK8 project started with a HTS complemented with the application of Hit Generation strategies. Several chemical series of CDK8-is were identified. After profiling of representatives from each series and multifactorial prioritization we selected a series of tricyclic CDK8-is for further HtL and LO phases. We have generated SAR/SPR data regarding primary activity, selectivity, in vitro ADMET and in vivo PK. This has allowed the identification of ETP-827 as our first selective orally bioavailable CDK8-i lead. ETP-827 has been used to generate antiproliferation data in a panel of +40 tumoral cell lines, providing cell line sensitivity to our CDK8-i. Selected sensitive cell lines have been used to further profile ETP-827 in comparison with published competitors. Moreover, ETP-827 has been used in in vivo PK-PD and efficacy studies in tumor models with preliminary positive results. Additionally, we have generated x-ray structures of CDK8-CyC cocrystallized with selected CNIO CDK8-is, demonstrating a type I binding mode. The series has been protected with a patent application.

INNOVATIVE ASPECTS

- The competitive landscape shows the absence of CDK8 inhibitors in advanced development phases nor in clinical trials. However, it is an active field of research in which some academic DD players and pharma companies are involved. It could be considered as an attractive scenario with clear possibilities to position CNIO CDK8-is as first in class compounds. Moreover, some of our CDK8-is also inhibit a secondary target which could be a positive differentiating factor versus competitors. Thus, ETP-827 has demonstrated to be superior in antiproliferation assays in selected sensitive cell lines.

IPR

The advanced chemical series represented by ETP-827 has been protected with an international patent application which will reach PCT public status in August 2016.

PARTNERING OPPORTUNITIES

At this point in the process we seek for pharma or biotech partners in order to license these data-packages and assets for further regulatory and clinical development at the pharma company. Co-development agreements are not excluded. In fact our preferred scenario will be that in which the participation of ETP-CNIO or other CNIO scientist could be taken into account as an added value for the development of CNIO originated compounds.

CNIC-CLINIC

PROFILE

CNIC and **Fundació Clinic** per la Recerca Biomèdica are both co-owners of the described invention. Our research is focus on the development of new therapies and the use of noninvasive imaging (particularly magnetic resonance) for the treatment, diagnosis and monitoring of Pulmonary Hyopertension PH.

SPEAKER

Ana García-Alvarez is a cardiologist trained at the Hospital Clínic (Barcelona 2004-2009) and further specialized in advanced cardiovascular imaging at the Mount Sinai Hospital (New York 2009-2010) and translational research at the CNIC (2011-present). She also has extensive training in research methodology (Master's Degree in Statistical Sciences from the Universidad Autónoma de Barcelona 2004-2008, and Series of Statistics and Epidemiology at the Johns Hopkins Bloomberg School of Public Health 2010-2011). She currently combines her work as a clinical cardiologist at the Heart Failure Unit at Hospital Clínic with her role as a translational researcher in the Department of Cardiovascular Imaging and Population Studies at CNIC in collaboration with Dr. Borja Ibañez and Dr. Valentin Fuster. In the last six years, her research has focused on pulmonary hypertension (PH) and she currently leads a number of research lines on PH.

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PRODUCT

β3-adrenergic receptor agonists (β3AR agonists)

MECHANISM OF ACTION

There are two major classes of β3AR agonists, the phenylethanolamines (comprising BRL37344, SR58611A, and CL316243) and aryloxypropanolamines (including mirabegron, cyanopindolol and CGP12177A). Distinctive pharmacodynamic properties of β3AR, such as their upregulation in disease and resistance to desensitization, suggest that they may be attractive targets for therapeutic intervention.

Like other adrenoreceptors, β3AR are coupled to G proteins. The downstream pathway activated by β3AR includes nitric oxide synthase (NOS), NO-activated guanylyl cyclase and cGMP synthesis, and increased cAMP synthesis.

Loss of cGMP and cAMP signaling is a hallmark in PH. Within the pulmonary circulation, cyclic nucleotides are responsible for mediating endothelin-dependent dilatation, thereby maintaining pulmonary vascular homeostasis, but they also have salutary actions on pulmonary vascular remodeling, fibrosis, and right ventricular (RV) function.

TARGET INDICATIONS

β3AR agonists, particularly mirabegron (Betmiga®), are currently used for the treatment of hyperactive bladder syndrome. However, our research focuses in the use of β3AR agonists for the treatment of ***chronic pulmonary hypertension***.

CURRENT STATUS

- Several experimental studies have shown that in vivo treatment with BRL37344, a β3AR agonist, improves cardiac performance and ameliorates myocardial injury in experimental models of heart failure and ischemia-reperfusion through a nitric oxide-mediated mechanism.
- In pulmonary vessels from dogs and rats, ex vivo β3AR agonists produces vasodilatation. This pulmonary vasodilator effect, added to the beneficial effect on ventricular remodeling, strongly suggests a potential therapeutic use of β3AR stimulation in PH due to HF.
- Our experimental preclinical research demonstrates that treatment with β3AR agonists produces a beneficial effect on hemodynamics, right ventricular remodeling and pulmonary vascular proliferation.
- An experimental study in pigs (n=34) with chronic PH created by pulmonary vein banding was designed to evaluate the acute hemodynamic effect and the long-term effect of β3AR agonists on hemodynamics, vascular remodeling and RV performance in chronic PH.
- Ex vivo human experiments were performed to explore the expression of β3AR mRNA and the vasodilator response of β3AR agonists in pulmonary arteries.
- Investigators of the Consortium are currently conducting a multicenter randomized clinical trial to assess the beneficial effect of mirabegron in patients with PH due to left heart disease.

INNOVATIVE ASPECTS

- Few therapies with high cost and limited beneficial effect are currently available for pulmonary arterial hypertension (group 1 in the current PH classification), and no pharmacological therapy has been demonstrated to have a consistent effect in PH due to left heart disease (group 2) or chronic pulmonary disease (group 3), which are the most frequent causes of PH.
- If proven beneficial, β3AR agonists would be the first pharmacological treatment for PH due to left heart disease or pulmonary disease.
- Distinctive pharmacodynamic properties of β3AR, such as their upregulation in disease and resistance to desensitization, suggest that they may be attractive targets for therapeutic intervention.

IPR

CNIC and Fundació Clinic per la Recerca Biomèdica, as co-owners of this invention, have filled in a related European patent application on August 29th, 2012 entitled "Beta-3 adrenoceptor agonists for the treatment of pulmonary hypertension" (WO 2014/033343). In 2015 this patent application has entered into national/regional phases in Europe, USA and Japon. Currently, it is under examination in the corresponding patent offices.

PARTNERING OPPORTUNITIES

CNIC and Fundació Clinic per la Recerca Biomèdica are interested in the collaboration with Industry to further continue the clinical trials development of this new therapeutic approach and the subsequent license agreement for use and exploitation.

CNIC

PROFILE

The B Cell Biology Lab is focused on the molecular and cellular events that take place in germinal centers - microstructures generated by B cells during immune responses. Our interests cover basic aspects of B cell biology, including the DNA remodeling associated with antibody diversification by the enzyme AID in germinal centers, the regulatory programs driven by microRNAs in germinal centers, and the generation of animal models to explore the impact of these events on the etiology of disease, most notably in inflammation and cancer. Our recent work has shown that microRNAs contribute to immune tolerance, and that individual microRNAs play critical roles in the regulation of germinal centers and can act as oncogenes or tumor suppressors. In addition, we have developed mouse models to study different regulatory aspects of AID activity in vivo. Finally, we are characterizing the functional contribution of antibodies and their diversification to atherogenesis.

SPEAKER

Antonio J. Quesada, PhD. Scientific Manager at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC). BS in Biochemistry at Universidad de Granada in 2000, and PhD with First Class Honors distinction at Universidad Autónoma de Madrid in 2005. Visiting Scientist at Northwestern University Chicago in 2003. Expert in R&D Management and regulations. Experienced in Grant Management, strategic planning and strategic decision-making processes. Dr. Quesada is University Expert in Management and Administration of Foundations, and Master in Direction and management of Foundations and NGOs by the UAM..

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PRODUCT

MIRacle (miRNA mimic) to treat Non-Hodgkin lymphomas

MECHANISM OF ACTION

MIRacle is a miRNA mimic, i.e. a molecule designed to mimic endogenous mature miRNAs, harbouring a chemical modification that improves their stability and biological efficiency. Moreover, we made use of MIRacle to treat BL xenografts and found that both intratumoral and intravenous injection promoted a consistent regression of tumors.

We first used inducible lentiviral versions of MIRacle to deliver the molecule to BL and DLBCL cell lines, and consistently found that MIRacle replacement impaired lymphoma growth. Secondly, we developed in vivo xenograft models and found that reintroduction of MIRacle in BL and DLBCL cells led to a dramatic block of tumor growth and extended mouse survival. Molecular analyses showed that the mechanism of action of MIRacle involved a decreased proliferation rate and an increased death of the lymphoma cells. Notably, re-expression of MIRacle not only interfered with tumor growth, but also promoted the regression of established tumors.

TARGET INDICATIONS

Non-Hodgkin lymphomas (NHL) are high prevalent diseases in western countries and their treatment these has a great economic impact. Diffuse large B cell lymphoma (DLBCL) is the most common lymphoid malignancy in adults, accounting for 30-40% of all NHL in western countries, and is often treated with R-CHOP (Rituximab-Cyclophosphamide, Doxorubicin, Oncovin, Prednisolona). We aim to develop a cheaper and more effective therapeutic

alternative for NHL with a particular interest in DLBCL. If successful, it can render extremely high benefits in terms of diminishing the relative cost of the treatment and of improving the life quality and survival of patients. In addition, our proposed therapeutic approach aspires to be the "treatment of choice" in NHL patients not responding to R-CHOP therapy.

CURRENT STATUS

- To directly address the effect of MIRacle for the treatment of primary B cell lymphomas rather than lymphoma cell lines, we took advantage of the lambda---myc transgenic mouse model, a mouse strain carrying a genetic modification that drives the generation of mature B cell lymphomas that very closely resemble the human BL disease.
- We treated lambda-myc tumors with MIRacle by intratumoral or intravenous injection and found that both routes of administration drove efficient regression of tumor growth. These results show that i) MIRacle is amenable to use in its synthetic form and both by local and systemic administration and that ii) primary B cell lymphomas are sensitive to MIRacle treatment.
- We are now starting an ERC Proof of Concept Grant to establish MIRacle toxicity in vitro and in vivo. Lymphoma cells will be treated in vitro with MIRacle and cellular parameters of toxicity will be assessed, including cell proliferation and cell death.
- In addition, MIRacle will be administered intravenously into wild type mice and complete histopathological and biochemical toxicity analyses will be performed.
- We are also comparing MIRacle versus R-CHOP treatments. We will directly compare the efficiency of MIRacle and R-CHOP treatments in lymphoma cells in vitro and in mouse models, including xenografts and primary BL in the lambda-myc mouse strain.

INNOVATIVE ASPECTS

- microRNAs have arisen as very promising therapeutic tools for numerous pathological conditions. In addition, and in sharp contrast to R-CHOP (and also to other therapeutic approaches, like radiotherapy), microRNA-based therapeutics provides a higher level of specificity. Indeed, a number of microRNA inhibitors are already in clinical trials (i.e. miR-34 has been approved for the treatment of hepatocarcinoma). However, MIRacle will be the first therapeutic candidate with potential application to the treatment of B cell neoplasias. But the most important innovative component of MIRacle is that it aims at replacing the normal levels of its miRNA that were once lost by the tumor cells rather than at the broad elimination of B cells. In this regard, MIRacle can be considered a tumor suppressor that will be therapeutically restored in tumor B cells to expectedly exert the exact same regulation that it does in their normal counterparts. Therefore, we believe that the toxicity of MIRacle will be considerably lower than current strategies for the treatment of B cell neoplasias.

IPR

The patent application claims different miRNA compositions, as well as compounds that mimic these miRNA activity, including pharmaceutically acceptable carriers and the route of administration useful for the treatment of diffuse large B cell lymphoma (DLBCL).

PARTNERING OPPORTUNITIES

We are interested in a cooperation with pharma industry in the following aspects: Development of MIRacle formulations with higher activity; Co-development of the current patent portfolio generate a suitable product to license and further analyze in Clinical trials; licensing of the current patent portfolio.

IBIMA

PROFILE

Instituto de Investigación Biomédica de Málaga

Neuropsychopharmacology research group: biological bases of motivated behavior and the pathophysiology of its alterations. Lines; i) Biological bases of motivated behaviors. ii) Anatomical components of learning, reward, emotional and motivational control systems as well as the anatomy of cognitive systems during development and in disease models. iii) Development of animal and in vitro models of diseases such as addiction, obesity and diabetes. iv) Development of new drugs for the treatment of motivated behavior disorders, especially for drug addiction and obesity.

SPEAKER

Fernando Rodriguez de Fonseca is the Coordinator of the Therapeutic Area at the Biomedicine Research Institute of Malaga and Director of the research group in Neuropsychopharmacology associated to Mental Health Unit of the Regional University Hospital of Malaga. Professor of Psychology at the Complutense University of Madrid. Coordinator of the Spanish Network of Addictive Disorders (RTA ISCIII). Member of the Scientific Committee of the European Monitoring Centre for Drugs and Drug Dependence. Founding partner and head of preclinical research of a biotech company, Vivia Biotech S.L.

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PRODUCT

Novel conjugation of oleic acid with an amphetamine derivative (OLHHA)

MECHANISM OF ACTION

Action mechanism based on reducing ingestion, activating fat metabolism and reducing fat deposits, and antagonizing oxidative stress. Properties:

- Activates PPAR alpha, with greater affinity than fibrates, to assure deep hypolipidemic effects and activators of the metabolism of fats.
- Reduces fat deposition in the liver. Inhibits the expression of SCD1 (desaturase 1) enzyme, a fundamental mechanism in steatohepatitis.
- Intake reduction effect, thereby adding anti-obesity to their antisteatosic profile.

TARGET INDICATIONS

Prevention or treatment of alcoholic steatohepatitis or non-alcoholic steatohepatitis (NASH)

Additional indications: Other pathological condition or disease caused by fatty liver, either alcoholic or non-alcoholic. Obesity.

CURRENT STATUS

- In the in vivo trails carried out (in both chronic and acute), evidence of activity against steatohepatitis has been found, showing a reduction in the liver fat content and plasma triglyceride levels.
- Experiments have also shown an improvement in kidney function by reducing increased plasma levels of urea and the profile of hepatic transaminases in plasma, with a fall in ALT and AST.

- The compounds are accepted according to the Lipinsky rule. Safe pharmacological profile, no interaction with hERG, and no or only mild effects on the activity of the different isoforms of the hepatic cytochrome P450.

INNOVATIVE ASPECTS

- There are no effective treatments for this pathology apart from the use of classical fibrates.
- Clinical trials are being developed to market new drugs or nutraceutical products, including: natural PPAR alpha receptor agonists, consisting of polyunsaturated fatty acids present in fish oil, antioxidants and liposoluble vitamins, including vitamin D and resveratrol, new drugs (minority).
- This compound exploits a completely new action mechanism based on intake reduction, activating fat metabolism and reducing fat deposits, and antagonising oxidative stress.

IPR

The therapeutic indication is protected by International Patent Application. Publication Number: WO 2016/083646 A1. Priority date: 24/11/2014. International Search Report: No relevant documents concerning the invention.

PARTNERING OPPORTUNITIES

We are looking for a partner interested in a license and/or a collaboration agreement to further develop and exploit this innovative technology.

IMIBIC

PROFILE

IMIBIC MAIMONIDES BIOMEDICAL RESEARCH INSTITUTE OF CORDOBA

The research group is a multidisciplinary group and is working in several investigation lines. Regarding our product leads to the treatment of degenerative osteoarthritis we are developing various research projects with the aim to obtain the necessary information to enhance the industrial protection of the product and the requirements that will allow us to conduct a clinical trial in both, human and animals, patients with degenerative osteoarthrosis

SPEAKER

Dr. Juan R. Muñoz-Castañeda has 14 years as posdoctoral researcher. He has worked for University of Cordoba and he carried out his post-doc at the laboratory of Prof. Ann Canfield at the Manchester University, UK. He has a multidisciplinar experience in areas such as oxidative stress, hepatology, nephrology or regenerative medicine. Now he works for Andalusian National Health System in Reina Sofía University Hospital and Maimonides Institute for Biomedical Research from Cordoba (IMIBIC leading the investigation group "Vascular Calcification. Calcium Metabolism". He has published more 40 scientific papers. He leads and collaborates national and international investigation proposals and he has developed 8 patents.

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PRODUCT

Allogenic treatment for osteoarthrosis with a composition derived from adipose tissue mesenchymal stem cells.

MECHANISM OF ACTION

The product is patented. It is not cell therapy since the changes made on adipose tissue mesenchymal stem cells (MSC) do not allow the functioning of these cells. The patented modifications on MSC maintain the beneficial effects of stem cells therapies without the limitations of these. These changes allow their allogenic use, storage, rapid biodistribution and accelerates recovery of cells in the injured tissue. In addition, the patented changes eliminate fully all those associated with cell therapy so that the product proposes a revolutionary concept of regenerative medicine.

At the moment the mechanism of action in the context of degenerative osteoarthrosis has not been documented. However we have published papers demonstrating the mechanisms of action in fulminant liver failure in rats. We observed that our composition derived from mesenchymal stem cells is anti-apoptotic, promotes proliferation and contains important cytokines and miRNA related to regeneration, proliferation and inhibition of apoptosis. We consider that these same mechanisms could be involved in the regeneration of cartilage during degenerative osteoarthrosis.

TARGET INDICATIONS

Previously this product was effective in the context of fulminant liver failure (data patented and published). Now our product has been tested and has quantifiable data for the treatment of degenerative osteoarthrosis with excellent results.

Moreover, this product has been also administered in animals (dogs and horses) with other musculoskeletal injuries such as breakdown muscle fibers or no union defects with positive results. We are confirming the effect on these other pathologies and propose to study its effect on other lesions muscleskeletal injuries.

In summary, we have developed a product with a very powerful capability to promote and enhance celular regeneration in the context of muscleskeletal pathologies.

CURRENT STATUS

We already have obtained important results showing in dogs (n=30) with degenerative osteoarthrosis. The efficiency of a single intraarticular infusion was observed during one year improving movements, pain and quality of life. Now we are setting up a start-up in an early state and we are collecting information related to the necessary requirements (from EMA, FDA) to perform a clinical trial in patients (animals and human). We have received funding from Carlos III Institute (Technological development proposal) to promote a clinical development of the product. In addition to degenerative osteoarthrosis we want to extend the beneficial effect of our product to other pathologies as for example breakdown fibers in sport medicine.

INNOVATIVE ASPECTS

- This is a new alternative therapeutic method based in stem cells but it has not the adverse effects of the "conventional" cellular therapy.
- This product is allogenic, may be storage and distributed in 24 hours in any place, with reduced costs and wide margin of gain.
- A single injection is more effective than conventional autologous therapies with stem cells or plasma derived from plaquets.

IPR

We have a solid IP strategy, that's include national and international patents (PCT/ES2014/070497 and PCT/ES2015/070797) related to the use of our product for the treatment of fulminant liver failure and degenerative osteoarthrosis. In the next stages of the project we plan to enhance them with additional patents.

PARTNERING OPPORTUNITIES

Three different options: Funding for investment in star-up; Collaborations agreement with the research group; License agreement.

UAB - Hospital de Sant Pau

PROFILE

In cooperation with the team lead by Professor Antonio Villaverde (of the UAB and CIBER-BBN), we develop functional proteins and nanostructured protein materials biofabricated in cell factories. These items, produced by conventional, fully scalable recombinant DNA technologies, are aimed to solve therapeutic needs related to the cell-targeted drug delivery and release, specially focusing on metastatic colorectal cancer.

SPEAKER

Ramón Mangues is a Research Professor and leader of the Oncogenesis and Antitumor Drug Grup at the Research Institut of the Hospital de Sant Pau in Barcelona. He coordinates a multidisciplinary team of 16 basic and clinical researchers, who are integrated in the Spanish network of nanomedicine CIBER-BBN. R. Mangues is a Clinical Pharmacist and Molecular Biologist who worked for ten years at New York University Medical Center. He has specialized in models of metastases, preclinical drug development and the use of nanoparticles for targeted drug delivery. He is a board member of CIBER-BBN and IIB-Sant Pau. R. Mangues was co-founder and Scientific Advisor of Argon Pharma SL, a spin-off of the Hospital de Sant Pau. He also held research contracts with Merck and Co. and Laboratoris Esteve and is currently collaborating with Pharma Mar.

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PRODUCT

Novel nanoconjugate for the targeted treatment of metastatic colorectal cancer

MECHANISM OF ACTION

We have developed a novel, cell-targeted nanomedicine for more effective and less toxic chemotherapy of metastatic colorectal cancer cancers. The prototype consists of a self-assembling modular protein produced in bacteria by cost-effective, fully scalable recombinant DNA procedures.

Upon production in bacteria, this modular protein self-organizes as 15 nm-nanonoparticles avoiding renal clearance. These vehicles fully target metastatic cancer stem cells for internalization and serve as vehicles for antitumoral drugs upon chemical coupling. The nanoconjugates show a proper biodistribution and accumulation in tumor and metastatic foci upon systemic administration, in absence of remarkable toxicity.

We have identified a non-antibody protein ligand (the peptide T22) of the cancer cell-surface marker CXCR4, which is significantly overexpressed in colorectal, pancreatic and lymphoid cancers.

On this basis, we have developed a novel generic technological platform based on self-organizing, protein-only nanoparticles of 15 nm targeted to CXCR4+ cells, in which building blocks are T22-containing fusion proteins. Both self-assembling and CXCR4+ cell targeting and internalization are mediated by the peptide T22, that acting as an architectonic tag also promotes efficiently internalization of the whole nanoparticle and any attached drug.

TARGET INDICATIONS

Targeted chemotherapy of colorectal cancer and or other human cancers in which CXCR4 is overexpressed in the surface of stem cells, including leukaemia, breast, gastric, ovary, pancreas cancers and potentially glioblastoma. T22-based nanoconjugates might become a first-in-class medicine in metastatic cancer.

CURRENT STATUS

The prototype so far developed consists of a self-assembling modular protein produced in bacteria by cost-effective, fully scalable recombinant DNA procedures and containing the tumor-homing peptide T22.

Upon production in bacteria, this modular protein self-organizes as 15 nm-nanonoparticles, which fully target CXCR4+ metastatic cancer stem cells for internalization and that serve as vehicles for conventional antitumoral drugs.

Upon administration in colorectal cancer mice models, the drug-loaded vehicle accumulates in primary tumor and in metastatic foci, with no detectable occurrence in liver, kidney, brain and other organs, destroying primary tumor and dramatically reducing the number of metastatic foci in absence of remarkable toxicity.

INNOVATIVE ASPECTS

- Control of metastatic dissemination is an unmet medical need. Emerging drugs, which block molecular drivers in specific tumor types have a low therapeutic index and lead to marginal patient benefit, associated to severe severity toxicities.
- While passive vectorising in liposomal doxorubicin or albumin-paclitaxel is unable to fulfil a true cell targeting, our approach represents a fully novel and versatile concept overcoming these bottlenecks, as the developed vehicle is non-toxic, fully targeted intracellularly and allows the delivery of potent anticancer drugs in a very tissue-specific way.

IPR

The key element of our technology is the use in a specific nanoscale vehicle of the tumor-homing peptide T22 that promotes internalization of linked drugs into CXCR4+ cancer cells. Any vehicle containing T22 and an antitumoral drug is covered by WO 2012/095527 (patent extended to Europe, USA, Australia and Israel, still pending). Additional IP covering nanoconjugates comprising T22: (i) New therapeutic agents (T22 nanoparticles carrying a specific therapeutic agent). (ii) Specific nanocarriers (T22 nanoparticles built with a specific scaffold protein, etc). Patent filing of such new inventions is in progress

PARTNERING OPPORTUNITIES

Industrial partners to further develop the Technology through a license and co-development agreement. Our targets are Pharma/Biotech companies within oncology field willing to load the carrier with their own drugs of interest. We envisage offering non-exclusive licenses to several companies in parallel.