MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

XXIII Encuentro de Cooperación Farma-Biotech

Martes, 28 de noviembre de 2023

El Programa Farma-Biotech tiene por objeto establecer un punto de encuentro para 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 presente jornada, que hace la número 23 desde que se inició el programa en el año 2011, está enfocada a la presentación de proyectos de medicamentos innovadores desarrollados en distintos centros de investigación y pequeñas empresas *spin-offs*, que han sido seleccionados por su potencial y prometedor estado de desarrollo, dentro del ámbito de la investigación preclínica.

En esta jornada se presentarán y discutirán **ocho propuestas** que se considera han alcanzado un **grado de madurez** razonable, lo que permite estudiar posibles **acuerdos de cooperación** con la industria farmacéutica en condiciones ventajosas técnico-económicas. Consecuentemente, pensamos que esta jornada reviste especial interés para las compañías farmacéuticas invitadas, incluyendo responsables de sus **unidades de desarrollo de negocio** e inversiones.

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 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.

Esta jornada tendrá lugar de forma presencial en la sede de Farmaindustria en Madrid. Para cualquier duda o aclaración adicional por favor contactar con:

Amelia Martín Uranga

amuranga@farmaindustria.es

Tfno. 915159350

Agenda

El programa Farma-Biotech, patrocinado por FARMAINDUSTRIA*, 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
09:00	Recepción, contactos informales, café		
09:30 09:45	*Bienvenida y presentación de la jornada*		***Javier Urzay*** FARMAINDUSTRIA
09:45 10:15	*Nanopartícula dirigida a la resolución de la inflamación*	Ensayos preclínicos	***Carlos Zaragoza*** UNIV. FRANCISCO DE VITORIA
10:15 10:45	*Plataforma PRS, inmunomodulador preventivo de tormenta de citoquinas*	Ensayos preclínicos	***Pedro Lapuente*** PEACHES BIOTECH SL
10:45 11:15	*Terapia neuroresolutiva para SNC*	Ensayos preclínicos	***Rubén López*** UNIV. AUTÓNOMA BARCELONA
11:15 11:45	*Inhibidor directo de la proteína cMyc para terapia oncológica*	Clínica I	***Santiago Esteban*** IDP DISCOVERY PHARMA
	DESCANSO. Café y refrescos. Contactos informales		
12:00 12:30	*Péptido para tratamiento de NASH.*	Ensayos preclínicos	***Albert Palomer*** ENDOLIPID THERAPEUTICS SL
12:30 13:00	*Biomarcadores epigenéticos para el diagnóstico preciso de cáncer de tiroides*	Probado en pacientes	***Mario Fernández Fraga*** CSIC
13:00 13:30	*Modulador de latencia celular contra persistencia del cáncer*	Ensayos preclínicos	***Esther Riambau*** ONIRIA THERAPEUTICS SL
13:30 14:00	*Pequeña molécula capaz de silenciar la expresión de oncogenes*	Clínica I	***Carmen Plasencia*** AROMICS
	FINAL. Aperitivos y refrescos. Contactos informales		

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 28 de noviembre de 2023**

MINISTERIO DE CIENCIA E INNOVACIÓN
AGENCIA ESTATAL DE INVESTIGACIÓN

La plataforma tecnológica Española Medicamentos Innovadores cuenta con la Ayuda (PTR-2022-001255) financiada por MCIN/AEI/10.13039/501100011033

PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

PROFILE

The Research Group led by Dr. Zaragoza focuses on the search for novel molecular targets with diagnostic, prognostic and/or therapeutic utility for the treatment of cardiovascular diseases, including acute coronary syndrome, heart failure, and atherosclerosis. We are generating brand new nanoparticle-based compounds focused on targeting specific molecules elicited in response to myocardial ischemia with the goal of preventing and non-invasively molecular imaging target visualization to treat and prevent progression of disease.

SPEAKER

Dr. Carlos Zaragoza is a PhD in Genetics in 1996. Cardiology fellow, Cardiology Department Johns Hopkins Hospital 1996/2000. Group leader National Center for Cardiovascular Research (CNIC) (2006-2012). Full Professor Physiology and Cardiology, University Francisco de Vitoria School of Medicine, and head of the Cardiovascular Research, Department of Cardiology, Hospital Ramón y Cajal, Madrid.

c.zaragoza.prof@ufv.es

PRODUCT

NIL10: a novel nanotechnological compound to reduce inflammation and preserves heart function after acute myocardial infarction

MECHANISM OF ACTION

NIL10 is capable of binding to immune cells expressing IL-10 receptor inducing this way a change in their behaviour while immune responses have started. NIL10 has demonstrated the powerful of inducing macrophage polarization towards resolutive phenotype by activation of anti-inflammatory factor STAT3.

It represents a noteworthy nanoparticle that adopts a liposome-based structure. It is conjugated with an analogue of IL-10 peptide, which confers the remarkable ability to effectively bind to IL-10 receptors, subsequently inducing immune cell regulation and bestowing anti-inflammatory characteristics. This lipid nanoparticle exhibits valuable therapeutic properties, particularly in the context of inflammation control.

In addition to its inherent attributes, we have introduced two supplementary components to enhance the versatility of NIL10. Firstly, the incorporation of a contrast agent facilitates precise tracking of the nanoparticle's in vivo performance using magnetic resonance imaging (MRI), enabling real-time monitoring of its distribution and interactions within the biological system. Secondly, the integration of a fluorophore serves as a vital tool for conducting histological studies and conducting biodistribution analysis, thereby providing crucial insights into NIL10's dispersion and localization within the body.

TARGET INDICATIONS

NIL10 has demonstrated cardiac protection after acute myocardial infarction following cardiac ischemia/reperfusion by inducing anti-inflammatory effects, which also opens a new window for its use to treat other cardiovascular inflammatory diseases.

CURRENT STATUS

- Intravenous administration of 1 mg/kg NIL10 induced cardiac protection of wild-type and IL-10 knockout mice and pigs subjected to Acute Myocardial Infarction.
- Cardiac protection was not induced in IL-10-receptor null mice, as shown by a significant recovery of cardiac function, in which inflammatory foci and fibrosis were strongly reduced, together with the finding that resolving M2-like macrophage populations were increased after day 3 of reperfusion.
- In addition, anti-inflammatory cytokines, including IL-4, IL-7, IL-10, IL-13, IL-16, and IL-27 were also elevated.
- Mechanistically, NIL10 induced activation of the IL-10 receptor/STAT-3 signalling pathway, and STAT3-dependent inhibition of nuclear translocation of pro-inflammatory NF-kB transcription factor.
- Next steps are focused on achieving compliance with GMP and GLP requirements, ensuring that the preclinical phase attains the necessary robustness to transition into the initial clinical trials successfully.

INNOVATIVE ASPECTS

- The primary achievement of our work lies in the vehiculation of this synthetic peptide, which allows for an increase in biocompatibility, prolonged action period of the compound, and enhanced in vivo half-life, while simultaneously reducing toxicity, side effects, and immunogenicity.
- Additionally, the incorporation of a contrast agent into its structure enables this compound to be employed not only for therapeutic purposes but also for diagnosing cardiovascular events.
- In essence, NIL10 emerges as a highly promising nanoparticle, poised to revolutionize inflammatory disorder treatments. Its specific targeting of immune cells and its traceable nature augur well for advancing medical research and potentially revolutionizing the landscape of anti-inflammatory therapeutics.

IPR

The compound is protected by a PCT patent, which is an international application that facilitates the process of seeking patent protection in multiple countries.

PARTNERING OPPORTUNITIES

Open to different proposals: from Licencing, M&A or Joint-Venture to milestones & hits driven agreements.

PROFILE

CÁTEDRA
en terapias avanzadas basadas
en secretomas celulares

UAM Universidad Autónoma de Madrid | Peaches BIOTECH

Peaches Biotech is focused on the generation of allogeneic drugs with tissue-selective immunomodulatory capacity, so as to limit the generation of fibrosis as much as possible, indirectly enhancing the regenerative capacities of the tissue. These types of drugs are applicable to a large number of diseases that involve inflammation and for which there is currently no highly effective drug. It is noteworthy that the company has its own factory authorised by the AEMPS for the production of this type of complex biological medicines under GMP conditions, demonstrating a high level of industrialization in their production.

SPEAKER

Dr. Juan Pedro Lapuente holds a degree in Medicine and Surgery from the University of Zaragoza, a PhD in Medicine from the Catholic University of Murcia (UCAM), a Master's Degree in Molecular and Cellular Biology from the University of Zaragoza, a European Master's Degree in Transfusion Medicine and Advanced Cellular Therapies from the Universities of Liège and the Autonomous University of Barcelona and is the author of the PRS patent.

p.lapuente@peaches.es

PRODUCT

PRS secretome tissue selective immunomodulatory complex (Biological medicinal product)

MECHANISM OF ACTION

PRS is an allogeneic drug composed of a tissue-selective complex secretome produced by indirect contact of M2 polarised macrophages with different cell types, depending on what is to be produced (allogeneic MSC from fat to produce PRS CK STORM), tenocytes (PRS TENDON), myocytes (PRS MUSCLE), Schwann cells (PRS NEUROPATIC PAIN), osteoblasts (PRS OSTEO), etc.

The complete characterisation of PRS products carried out through close collaboration between the company Peaches S.L. and the AEMPS, within the framework of the UAM-Peaches chair, has allowed to define the different mechanisms of action of the different types of PRS, although it can be stated generically that they all act by immunoregulation of the innate immunity through immunoregulation of the TLR pathways, especially affecting TRAF-6, Nf-kβ and NLRP3 (down-regulating their activity), resulting in better and faster communication and coordination with the adaptive immune system, as well as anti-inflammatory immunomodulation through the purinergic system, mainly affecting P2X7 receptors (decreasing their activity) and A3 and A2a receptors (increasing their activity). All this promotes a rapid anti-inflammatory, analgesic, antifibrotic and proregenerative effect.

TARGET INDICATIONS

The platform allows the production under GMP conditions of different types of allogeneic PRS for different tissues and indications. The currently most developed are PRS CK STORM (indicated in the control of cytokine storm associated with COVID-19, pancreatitis, moderate/severe sepsis or Chron's torpid ulcer), PRS MUSCLE (indicated in muscle ruptures), PRS TENDON (indicated in tendinosis), PRS NEUROPATIC PAIN (indicated in chronic neuropathic peripheral nerve pain), PRS OSTEO (indicated in acute rib fracture).

CURRENT STATUS

- Currently, the company has obtained authorisation for several master cell banks of different cell types, as well as a GMP manufacturing plant for biological drugs and advanced cell therapy drugs, which allows it to manufacture large quantities of the different PRSs mentioned above through its indirect contact co-culture platform.
- The permanent collaboration framework with the AEMPS through the UAM-Peaches chair has resulted in a very clear roadmap on how to bring the different types of PRS to the EECC, with agreed protocols on how to characterise, formulate, present, etc... each of them.
- The company is currently about to submit through the CTIS platform two clinical trials with the PRS CK STORM in two different indications (one for the control of cytokine storm associated with moderate/severe sepsis, and another for the treatment of torpid ulcer associated with Chron), and expects to submit 4 more applications in 2024 for other types of PRS in different indications (acute rib fracture, chronic neuropathic peripheral nerve pain, acute muscle rupture and tendinosis).

INNOVATIVE ASPECTS

- The use of a complete secretome to treat inflammation, unlike single-target anti-inflammatory drugs (single or few therapeutic targets), has the advantage of covering all the pathways by which inflammation is established and maintained over time, acting through immunoregulation of the purinergic system and all TLR systems.
- This means that all PRS products have a high tissue-selective anti-inflammatory potency with a very high biosafety profile and high efficacy, achieving maximum pain reduction in a few hours, avoiding the dreaded fibrosis and favouring an accelerated regenerative process that can even lead to the regeneration ad integrum of the tissue affected by the inflammation.
- With respect to cell therapies, its advantages are evident, given that it is a cell-free therapy.

IPR

Currently the European patent has just been finally granted and the worldwide PCT is in the national phases.

PARTNERING OPPORTUNITIES

The company Peaches S.L. is looking for one or more strategic partners, who will provide, in addition to capital, their know-how in the world of the pharmaceutical industry, both in terms of their capacity to carry out phase III trials and to commercialise the products in the future.

PROFILE

UAB
Universitat Autònoma de Barcelona

Whitin the UAB, this **Research Group** has the following lines of research: neuroinflammatory response in neurodegeneration induced by lesions or diseases of the central nervous system; cellular and molecular mechanisms involved in degenerative diseases of motor neurons in experimental models; cell therapy by transplantation of mesenchymal stem cells and stem cells for the repair of spinal cord injuries and degenerative diseases of motor neurons; therapies to improve axonal regeneration and functional recovery after peripheral and central nerve injuries; pathophysiological mechanisms of neuropathic pain induced by nerve and spinal cord injuries and therapeutic strategies; and study of the cellular and molecular mechanisms involved in demyelinating diseases.

SPEAKER

Rubén López-Vales is a full professor at Universitat Autònoma de Barcelona. He has a solid scientific career in the field of neuroinflammation. His research team has identified several mediators that are involved in the initiation and resolution of the inflammatory response after injuries or diseases of the nervous system and that their modulation promotes therapeutic actions. He has recently been awarded an ICREA Academia award.

ruben.Lopez@uab.cat

PRODUCT

Maresins as a new treatment for injuries and diseases of the nervous system

MECHANISM OF ACTION

Inflammation is the immune system's way of responding to infection or injury. Normally inflammation is resolved which allows healing and recovery of the tissue. In neurodegenerative conditions, inflammation can be excessive or chronic and can overwhelm the immune system's ability to resolve the inflammatory response.

Maresins are new molecules that stimulate the body's natural mechanisms to resolve inflammation in host tissues, without leading to immunosuppression. Maresins mediate this effect by silencing pro-inflammatory mediators, inactivating signaling pathways that promote inflammation, removing immune cells from tissues, shifting the immune cell phenotype from a pro-inflammatory to an anti-inflammatory state, and by promoting tissue repair.

Maresins are lipid mediators synthesized by immune cells in inflamed tissues, especially macrophages, that orchestrate the resolution of inflammation, tissue repair and the recovery of tissue homeostasis. These maresins are not synthesized in the nervous tissue of patients suffering from diseases of the nervous system such as amyotrophic lateral sclerosis, multiple sclerosis or Alzheimer's, among others, which leads to the chronic inflammatory response characteristic of these pathologies. Moreover, the administration of maresins reduces neuroinflammation and promotes therapeutic effects.

TARGET INDICATIONS

A new treatment to limit neuroinflammation in various degenerative disorders such as acute spinal cord injury, multiple sclerosis and amyotrophic lateral sclerosis (ALS).

CURRENT STATUS

- Our studies demonstrate great efficacy of the administration of maresins for the treatment of acute traumatic injuries of the spinal cord, as well as, for demyelinating lesions (multiple sclerosis) and motor neurons diseases (amyotrophic lateral sclerosis).
- Currently, most non-regulatory experiments have been conducted, including dose-response studies; mechanisms of action studies, comparative efficacy studies with other competing drugs, in vivo toxicology studies, formulation studies for oral and intravenous administration, pharmacokinetic studies, and trials in large animal.

INNOVATIVE ASPECTS

- Current therapeutic strategies to treat inflammation and its collateral damage in tissues have not changed conceptually since ancient healers, since they are based on suppressing, blocking or inhibiting the mediators that initiate inflammation. Although many of these drugs are effective in treating acute inflammation, they have very limited efficacy in diseases with persistent inflammation, a hallmark event in injuries and diseases affecting the central nervous system (CNS).
- Importantly, prolonged use of anti-inflammatory drugs results in severe immunosuppression that often leads to opportunistic infections and the development of cancer, among other side effects.
- Our strategy for limiting inflammation is based on a paradigm shift in how to treat inflammation, as it focuses on stimulating the body's natural mechanisms to resolve excessive inflammation without suppressing the immune system's ability to respond to new infections or injury.
- We have demonstrated its therapeutic potential in relevant animal models for the three proposed indications without leading to immunosuppression or toxicity.

IPR

A strategy of protection of the technology has been followed through two patents for the use of maresins and other resolving lipids in neurotrauma (WO2019016580A1) and neurodegenerative and demyelinating diseases (WO2010033509). These patents were filed in 2017 and 2018, respectively, to cover major markets. These patents have recently received authorization in the U.S. and are currently pending review in other territories.

PARTNERING OPPORTUNITIES

it has been contacted several pharmaceutical companies so far. A possible license of the assets has been put on the table for one or all the indications that are considered in this project. It has aroused quite remarkable interest, leaving a possible license or co-development in the project pending receipt of additional results that advance the TRL. We believe that we have already done so and that is why we are proposing this possible collaboration now. The event in which we will participate seems to us an optimal starting point for this aim.

PROFILE

IDP Pharma is a clinical stage biotechnological company that develops therapies to treat incurable diseases, including cancer and beyond. The company is focused on developing first time ever drugs targeting a fundamental class of disease drivers, intrinsically disordered proteins (IDPs), thanks to its novel intrameticsTM platform. The company has licensed two assets (EU and USA biotechs) and partnered with a EU pharmaceutical company to exploit IDP's products beyond cancer, including ophthalmology, dermatology and respiratory diseases.

SPEAKER

Dr. Santiago Esteban got his Ph.D in chemistry at the Institute of Molecular Science (Spain) and has worked at several international institutions (KIT, Groningen Institute of Biotechnology, IRB). Dr. Esteban managed IDP Pharma since its foundation in 2015, focusing on strategic growth, business development and investors' relations. He is an expert in IDPs and has devoted 15 years to develop technologies to study this undruggable class of targets (8 years within IDP Pharma).

s.esteban@idp-pharma.com

PRODUCT

IDP-121, a first-in-class drug blocking and degrading cMyc oncoprotein

MECHANISM OF ACTION

The nonclinical pharmacology studies elucidated the full MoA of IDp-121, which involves binding to monomeric cMyc, preventing its activation and prompting it for degradation. IDP-121 induces cell cycle arrest and fast apoptosis of tumour cells while healthy cells are barely affected.

Histopathological analysis of tumor tissue provided direct evidence for in vivo target engagement in murine xenograft models of MM and lung cancer. On-target effect last at least 3 days after a single administration. IDP-121 is fully stable in plasma and liver

TARGET INDICATIONS

IDP-121 is approved by AEMPs to start Phase I/II in haematological cancers (MM, DLBCL, CLL). IDP121 is also efficacious (in vivo) in solid tumours dependent on cMyc, such as NSCLC and SCLC. Other indications include for example polycystic renal disease (APKD) and idiopathic pulmonary fibrosis(IPF)

CURRENT STATUS

- IDP-121 is a first-in-class synthetic drug manufactured under GMP/GLP conditions (based on peptidomimetic technologies). The drug product is a solution for injectable, the manufacturing cost is low and the clinical batch of the drug product is released.
- All the pre-clinical and GLP toxicology studies have been successfully completed. It has been approved by AEMPS to start first-in-human clinical trials.
- The clinical plan approved by AEMPS includes a dose escalation (Phase I) and an expansion phase (Phase II) in hematological cancers (Multiple myeloma, CLL and DLBCL).
- The drug product is released, and 4 hospitals are recruiting patients. To comply with Regulatory Authorities for the approval of clinical trials, a 28-day GLP toxicology and safety pharmacology study in rats and minipigs was completed.

- Unlike most anticancer drugs, a NOAEL was determined in both species.
- Importantly, there was no systemic tissue or target organ toxicity associated with IDP-121, including no effects on rapidly proliferating tissues such as bone marrow or gastrointestinal, frequently adversely affected by oncology drugs.
- There were no findings in the toxicology studies that prevents progression of IDP-121 into clinical testing.

INNOVATIVE ASPECTS

- IDP-121 presents high in vivo potency in a variety of tumours and present synergies with SoC.
- It is the first cMyc direct inhibitor/degrader in clinical stage of development. Thus, it represents the first therapy that addresses the underlaying driving force of several haematological cancers.
- For example, multiple myeloma remains incurable and despite adoption of novel and costly therapies (i.e. CART), patients ultimately relapse and became refractory.
- No approved drug is directed to the underlaying disease cause, cMyc, which explains the recalcitrant behavior of the disease. IDP-121 solves this. The candidate is a synthetic molecule, thus low COGs, and it benefits from a biomarker to stablish an optimal biological dose.
- IDP-121 lacks common toxicities of anticancer agents, priming it for combination.

IPR

IDP-121 is protected by 4 patents (composition of matter) in 8 countries (USA, EU, Canada, AUS, China, Korea, India and Japan), two of them already granted at international level (USA, EU, China, Australia, etc). Patents filed in 2016-2018.

PARTNERING OPPORTUNITIES

IDP Pharma is seeking partners to codevelop or license IDP-121, in addition to partnering its platform across several therapeutic areas.

PROFILE

Endolipid is a spin-off from the Vall d'Hebron Research Institute (VHIR) associated to the Research Group on Diabetes and Metabolic Diseases. The company is focused on the development of a new platform to generate SHBG-mimic peptides for the reduction of ectopic fat. The platform has produced to date two peptides, EDL6D to treat NASH and EDL81 to treat cellulite. EDL6D is in preclinical development while EDL81 has been licensed to a derma company.

SPEAKER

Albert Palomer holds a PhD in chemistry by the Univ of Essen and the Max Planck Inst. and has gained +30 years expertise in drug development in pharma companies Ferrer and Menarini as well as in start-ups as CEO of Endolipid and Abac Therapeutics. AP has co-discovered 2 marketed drugs: The analgesic Enantyum® and the antibiotic Ozenoxacin® and serves as advisor and board member in 4 start-ups. AP is co-author of 34 patents of which 3 are in operation.

apalomerbenet@gmail.com

PRODUCT

SHBG-mimic peptide EDL6D

MECHANISM OF ACTION

EDL6D is a novel drug candidate currently in preclinical development for the treatment of NASH with a new mechanism of action and an innovative therapeutic approach. The peptide EDL6D has been validated in vivo in NASH mice models with an effect in lipolysis, lipogenesis, fibrosis and inflammation, superior to development drugs.

SHBG is a hepatic glycoprotein that transports sex hormones and also has effects on lipolysis, lipogenesis, fibrosis and inflammation in the liver. Because of these 4 effects, SHBG protects mice against the development of NASH and represents a new and differentiated therapeutic option. The protective effect of SHBG has been validated by the research team at VHIR using a transgenic mouse expressing human SHBG.

The SHBG is downregulated in fatty liver, thus, the in vivo effect of the SHBG-mimic peptide not only completes the validation of SHBG as a new therapeutic target but also represents a new approach to treat NASH by restoring the diminished SHBG functions.

TARGET INDICATIONS

EDL6D is intended to be used for the treatment of fatty liver and NASH (NAFLD/NASH) during all states of the disease, namely, in the early phases where fatty liver predominates (NAS F0-F2) and in the advanced ones with established fibrosis (F3-F4). SHBG levels are reduced in obesity, diabetes and PCOS, thus, EDL may apply in any of these diseases. In fact, the company is already exploring the application in PCOS.

CURRENT STATUS

- EDL6D is a peptide with proof-of-concept demonstration in in vivo mouse models in which has shown to reverse the effects of fatty liver and protect against the onset of the disease. EDL6D reduces steatosis, fibrosis and inflammation, the main causes of the disease.

- The effect has been demonstrated by measuring endpoints in histopathology (cumulative Brunt score), lipid content (TAG), AST/ALT, expression of biomarkers like lipogenic enzymes/receptors (PPARg, ACC, ACLY and FAS), fibrosis biomarkers (TGFb, Coll1A1, Coll3A1) and inflammatory cytokines (F480, TNFa, IL-1b, -12 and -6). The peptide EDL6D has been selected for preclinical regulatory development.
- EDL6D has also shown notable effect in vitro in human hepatic cells and adipocytes. Taken together, the in vivo results in mice and the in vitro data in human cells suggest that EDL6D may show notable clinical efficacy. Moreover, in combination with the observed safety profile, it may represent a new and differentiated therapy for NASH.
- The new MoA and the protective effect of SHBG has been validated using a transgenic mouse expressing human SHBG by the research team at VHIR (published data)

INNOVATIVE ASPECTS

- SHBG protects against fatty liver, but the hormone is downregulated in this pathology. The SHBG-mimic peptide EDL6D restores the SHBG functions, thus, represents a novel approach to the disease treatment with notable differences compared to current ones.
- It is an unexplored MoA that mimics a natural protection against the disease.
- It reduces the multiple causes of the disease (steatosis, fibrosis and inflammation), thus, it is expected to show greater clinical efficacy with special emphasis on fibrosis.
- EDL6D mimics an endogenous protein, thus, it is expected to show minor side effects.
- It is a natural-driven mechanism that restores the diminished SHBG protective action.

IPR

EP3003351B1 and US10729634B1 (priority 2013) granted in EU and USA. PCTEP2022084303 (priority 2021) Product patent for lipolytic peptides. EP23382535-5 (priority 2023) Product patent for SHBG mimetic peptides in NASH.

PARTNERING OPPORTUNITIES

The research team at VHIR is widely experienced in performing clinical trials under industry standards, however, having the guidance of Pharma guarantees the focus and quality according to pharma industry that will be ultimately the receiver of the product.

PROFILE

The laboratory is currently leading multiple lines of research focused on the study of epigenetic mechanisms governing physiological / pathological conditions. These lines involve a complex interplay between experimental models and state-of-the-art computational approaches. 1) Exploration of the intricate relationships between ageing and cancer from a molecular perspective. 2) Identification of molecular vulnerabilities and diagnostic/prognostic biomarkers in human cancer. 3) Environmental epigenetics involved in learning and cognitive decline.

SPEAKER

Mario Fernández Fraga is a Research Professor at the Spanish National Research Council (CSIC) and leads the Cancer epigenetics laboratory at the Nanomaterials and Nanotechnology Research Center (CINN). His lines of research focus on the study of epigenetic mechanisms that govern the relationship between ageing and cancer, with special emphasis on the discovery of new biomarkers relevant to the diagnosis of human diseases.

mffraga@cinn.es

PRODUCT

Thyromethyl, a method for the diagnosis of thyroid cancer based on epigenetic biomarkers

MECHANISM OF ACTION

The mechanism of action of this machine learning-based classification system is based on the use of a Random Forest model-based prediction approach on a retrospective training cohort of 54 follicular thyroid samples analyzed with EPIC methylation arrays. This molecular classifier, based on only three epigenetic biomarkers, was subsequently validated by bisulfite pyrosequencing experiments.

The development of new orthogonal diagnostic approaches may improve the diagnostic accuracy of thyroid nodules and avoid unnecessary interventions, especially in cases involving indeterminate nodules, which account for up to 20% of all clinical observations.

TARGET INDICATIONS

This proposal is framed within the therapeutic area of Oncology and is particularly oriented towards the implementation of epigenetic biomarkers for the diagnosis of thyroid nodule malignancy.

CURRENT STATUS

- By analyzing the genome-wide genetic and epigenetic profiles of 54 biopsies from patients with suspected thyroid nodules, a diagnostic model based on machine learning techniques and a minimal number of molecular biomarkers has been developed that is able to discern with high sensitivity and specificity the malignant status of a given thyroid nodule.
- This methodology has been successfully tested in several retrospective and multicentric cohorts and has been analysed with different experimental methodologies, including methylation arrays and the bisulphite pyrosequencing technique.

- The use of these epigenetic biomarkers has been tested in a relevant clinical setting, including the analysis of more than 100 biopsies from patients with suspected thyroid nodules and at least 29 fine needle aspirations (FNA).

INNOVATIVE ASPECTS

- This method provides a complementary tool to improve preoperative diagnostic evaluation in order to prevent or prioritise thyroidectomies of thyroid nodules with undetermined diagnosis.
- The classification system, based on a minimum number of epigenetic biomarkers, is able to discriminate between benign and malignant nodules, improving previous molecular classifications based on genetic biomarkers.
- This method can be easily applied in clinical settings using simple pyrosequencing assays, and is robust against different sample acquisition techniques, whether biopsies or FNA.
- The method is cost-effective and has high accuracy, sensitivity and specificity, improving the specificity of other related studies.

IPR

This technology is protected by a priority European patent application filed in February 2022. Also, in February 2023 a PCT patent application was filed

PARTNERING OPPORTUNITIES

The preferred form of collaboration would be through a license and exploitation agreement. Alternatively, the establishment of a *spin-off* might be considered.

PROFILE

Oniria Therapeutics is a biotech company focused on the field of precision oncology. It develops first-in-class therapies to modulate and eliminate dormant tumor cells as a novel targeted strategy to overcome their persistence. Oniria is a Spin-off of Vall d'Hebron Institute of Oncology (VHIO), the University of Barcelona and ICREA. Its flagship product, ONR-001 is an oral small molecule that allosterically activates TET2, a master epigenetic enzyme, causing tumor cells to enter a dormant state and even die. It is indication agnostic and can be used at all stages of the disease.

SPEAKER

Esther Riambau is Co-Founder, CEO & Board Member at Oniria Therapeutics, S.L. She has over 19 years of experience in Technology Transfer including entrepreneurship, IP licensing, contract research, and business development. Mrs. Riambau has a mixed profile; she is biologist and biochemist and got an MBA. She is also Co-Founder at Gate2Brain, S.L.

eriambau@oniriatherapeutics.com

PRODUCT

ONR-001, first-in-class oral treatment to overcome cancer persistence

MECHANISM OF ACTION

TET2 is an epigenetic enzyme capable of transforming 5-methylcytosine (5mC) into 5-hydroxymethylcytosine (5hmC). The relationship between genome hypermethylation (DNA) and the onset and persistence of cancer has been demonstrated. TET2 demethylates the tumor genome, specifically activating disease-fighting tumor suppressor genes.

Oniria has identified TET2 agonists (ONR-001), which could be used in different clinical scenarios. These drugs can induce and sustain tumor latency for prolonging disease-free survival or eliminate persistent cancer cells to prevent relapse, respectively.

TARGET INDICATIONS

It has been identified relevant efficacies in melanoma, colorectal cancer (CRC) and acute myeloid leukemia (AML) animal models. It is expected to demonstrate efficacy in glioblastoma, ovarian tumor, and other ones where TET2 loss is crucial in the disease initiation.

CURRENT STATUS

- ONR-001 has demonstrated in-vivo efficacy in acute myeloid leukemia (AML), melanoma and colorectal cancer (CRC) models with high tolerability in rodents.
- Currently Oniria is selecting the final candidate that will enter Regulatory Preclinical phase in January 2024.
- We have already demonstrated efficacy in-vitro, ex-vivo and in-vivo.
- Our initial RNAseq studies on AML cells treated with ONR-001 show the induction of different tumor suppressors including p21, which is related with cell cycle arrest and apoptosis.

- ONR-001 is a small and safe molecule with optimal pharmacokinetic properties for oral administration.
- ONR-001 has already demonstrated low acute and sub-chronic toxicity.

INNOVATIVE ASPECTS

- ONR-001 is a patented oral small molecule, first-in-class, that allosterically activates TET2, causing tumor cell enter dormancy and apoptosis (cell death). TET2 once restored to function, demethylates DNA, reactivating other tumor suppressors, thus blocking tumor proliferation, and promoting apoptosis.
- Non-specific hypomethylating agents (HMAs) used to treat hematological cancers (Vidaza or azacytidine and Dagogen or decitabine) remain unsatisfactory in clinical practice due to their toxicity and unknown mechanism of action that prevents personalized precision cancer therapy. The competitive advantage of ONR-001 over them is its low toxicity.
- The specificity of ONR-001 for TET2 overcomes conventional HMAs' handicaps and opens a therapeutic window for patients with poor performance status or comorbidities who could not receive the standard treatment. In addition, this feature also opens a range of opportunities within solid tumors.
- The market for a TET2-specific demethylating agent such as ONR-001 is much larger than the market for a non-specific and highly toxic demethylating agent.
- On the other hand, Dacogen and Vidaza are intravenous drugs, while ONR-001 is intended to be an oral drug and therefore would also improve the route of administration and the treatment of patients could be at home, opening the door to chronic treatments and indications.

IPR

Patent TET2 agonists (ONR-001): EP21382343.8 "Compounds for use in the treatment of hyperproliferative disorders". EU priority application 04/21/2021. (Inventors: H.G. Palmer, I. Puig, J. Tabernero, D. Galdeano, D. Muñoz-Torrero, X. Barril and S. Ruiz). Current situation in PCT.

PARTNERING OPPORTUNITIES

Open to co-developments with pharmaceutical companies and to test better responses and synergies of ONR-001 with targeted and immune-oncology treatments. We have already identified efficacy in ageing indications. Open to co-developments in this field.

PROFILE

AROMICS is a privately-owned development stage biotech company founded in 2005 with strong experience on the implementation of personalized medicine approaches on the discovery and development of novel and improved therapies to combat human disorders like cancer. The company is pioneering the development of a new class of anticancer agents directly targeting on RNA and silencing this way, aberrantly expressed proteins in poorly responsive and aggressive oncology conditions. A focused discovery & initial preclinical program initiated six years ago that rendered a new family of chemical entities protected under granted patents. A first candidate is advancing into clinics due its efficacy, safety and pharmacological in a rare but aggressive tumor.

SPEAKER

Carme Plasencia is a Chemist (BsC), PhD in Medical Oncology, Master in Biotechnology and MBA. Over 25 years experience in drug discovery and development particularly in oncology field, working in public and private research centers in Spain and USA, Dr. Plasencia is currently the co-founder and CEO of AROMICS and co-founder and member of the board of several other small companies Acceleromics (for antivirals development) and Aesis Therapeutics (for anticancer agents). Speaker at national and international conferences about value creation, EU non-dilutive funding, IP and valorization, her vision pivots in the synergistic use of technologies and know-how for generating innovative products while implementing time and cost-efficient R&D structures.

carme.plasencia@aromics.es

PRODUCT

NAX035: A Berberine derivative for the treatment of cancer

MECHANISM OF ACTION

NAX035 bind to specific RNA pockets localized in promoter regions of oncogenes, silencing this way the expression of relevant proteins, drivers of the disease and whose overexpression is linked to poor prognosis and lack of response to treatments but whose silencing or modulation have proven challenging with other drug approaches and modalities.

The compound is a first candidate of the family of RNA ligands advancing to clinics, with potent antitumor effect in a variety of tumors, including but not limited to malignant mesothelioma, through direct effect on cancer cell growth, metabolism, immunomodulation and metastasis inhibition, that postulates it as real promising anticancer therapy.

NAX035 high potency is related to its mechanism of action: it abrogates the protein expression of a well-known and clinically validated target thymidylate synthase (TS), a central enzyme involved in DNA and RNA synthesis.

TARGET INDICATIONS

Compound addresses aggressive tumors which intrinsically or by way of acquired drug resistance, poorly respond to standard therapies. As per primary indication we address malignant mesothelioma, a rare and aggressive cancer in need of effective therapies. As second indication we have additional preclinical data in refractory ovarian cancer, colorectal and pancreatic cancer.

CURRENT STATUS

- NAX035 has completed the pre-IND package and GMP manufacture of drug substance.
- It has proven in vitro and in vivo efficacy in a variety of tumors, appropriate pharmacology, toxicology and safety and with a cost-effective and robust manufacture and simple formulation for parenteral and/or oral posology to be used in patients.
- NAX035 is currently progressing into clinical trials (Phase 1/2) to prove safety and efficacy in cancer patients in at least two indications including mesothelioma.

INNOVATIVE ASPECTS

- Compared to other drugs in mesothelioma, NAX035 supposes a revolutionary approach, with no other drug in market targeting the RNA of a predictive and prognostic target validated in the disease, which de-risks the clinical approach.
- It is a solution for a rare disease with overall 5-year survival rate below 10%, median survival of 14 months, PFS of 6 months and very limited options exist to treat patients particularly those non responding to chemo- or immune combinotherapies (~60%).
- NAX035 is eligible to obtain Orphan Drug Designation, with potential for key regulatory and commercial advantages.
- Compared to conventional TS inhibitors (usually by mimicking natural substrates or cofactors) that directly bind the protein and inhibit its activity, NAX035 is a first-in-class acting as "translational repressor" binding to the mRNA and silencing this way the expression of the protein. Thus, NAX035 activity or toxicity is not limited by levels of the protein and/or its natural substrate (dUMP) or cofactor (folate). Instead, RNA binding engage a whole deep effect involving cell signalling, cancer cell metabolism inhibition and retaining some beneficial attributes (anti-inflammatory and immune-priming) as per structure-activity relationship with parental compound berberine.
- It proved efficacy, safety and tolerability in animal models not inducing relevant haematological or biochemical side-effects.
- Finally, is effective when administered as single agent or in combination with other agents so remain an option for being used as first- or second-line therapy in refractory patients.

IPR

The following granted patents covers the technology: US Patent 8,188,109 B2 (granted in May 2012), JP 5,778,145 B2 (granted in September 2015) and EP patent 2,456,770 B1 (granted December 2016) and biphenyl derivatives family is in-licensed to the company.

Aromics retain ownership of whole patent in Spain (ES2617187T8).

End 2021, Aromics applied for a proprietary patent on manufacture process and additional patents are currently on preparation for extending IP in specific clinical uses.

PARTNERING OPPORTUNITIES

We are looking for specific partnerships to advance rapidly into clinical trials and scaling up into novel indecations while enriching the IP, financial and commercial visions, and/or are interested in potential licensing agreement.