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

XVII Encuentro de Cooperación Farma-Biotech

Proyectos avanzados

Miércoles, 28 de noviembre de 2018

La jornada 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 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 **nueve propuestas** para que realicen su presentación en la jornada del miércoles día 28 de noviembre en Madrid.

Seis de estos nueve desarrollos de fármacos pertenecen a pequeñas empresas biotecnológicas, y tres a instituciones públicas (un hospital y dos centros de investigación). **Todos ellos se encuentran en fases avanzadas y tienen interés en llegar a acuerdos de colaboración con compañías farmacéuticas que faciliten el interés mutuo.**

Farmaindustria viene siguiendo el desarrollo de aquellos proyectos que en su momento fueron calificados de forma muy positiva en una fase anterior, pero se consideró entonces que eran prematuros. Hoy día, **tras haber progresado notablemente en el desarrollo**, han llegado a completar fases preclínicas e iniciarse en Fase I/IIb, por lo que entendemos 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.

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
09:15 09:30	Recepción, contactos informales, café		
09:30 09:45	*Bienvenida y presentación de la jornada*		***Javier Urzay*** FARMAINDUSTRIA
09:45 10:10	*Ciclatop, fármaco para el tratamiento de la dermatitis atópica*	Completado ensayo clínico I/II	***Luis Ruiz Ávila*** Spherium biomed
10:10 10:35	*Nanopartículas de oro conjugadas a un péptido contra cáncer de pulmón y melanoma*	Preclínica completada en modelos murinos	***Carmen Álvarez*** Hospital Valdecilla
10:35 11:00	*Inhibidor de kinasa dual FLT3-PIM para Leucemia Mieloide Aguda*	Desarrollada fermentación a escala industrial	***Francisco Moris*** Entrechem
11:00 11:25	*Nuevo medicamento como primera línea frente al cáncer de endometrio y el cáncer escamoso de pulmón*	Iniciada fase clínica I/IIb	***Albert Marofà*** Ability Pharma
11:25 11:50	*Nuevo biomarcador en orina para el screening del cáncer de próstata, superior a PSA*	Resultados positivos excelentes, N=1300	***Raúl Miguel Luque*** IMIBIC
11:50 12:15	Café. contactos directos		
12:15 12:40	*Derivado de la berberina como agente antitumoral para tratamiento del mesotelioma maligno*	Primer compuesto lead que avanza hacia clínica	***Carmen Plasencia*** Aromics
12:40 13:05	*Tratamiento de la enfermedad de Alzheimer mediante vectores adenoasociados administrados por V.I.*	Desarrollando preclínica en sistemas vivos	***José María Frade*** Tetraneuron,SL
13:05 13:30	*Diagnóstico de demencia con cuerpos de Lewy y monitorización de tratamientos anti-agregatorios de alfa-sinucleína*	Validación incluye Parkinson y Alzheimer, N=120	***Katrin Beyer*** IGTP
13:30 13:55	*Fármaco remielinizante de administración oral para el tratamiento de la esclerosis múltiple*	Demostrada eficacia en tres modelos animales	***Ana Martínez*** Ankar Farma
14:00- en adelante	*Aperitivos. 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: **Miércoles día 28 de noviembre de 2018**

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

La Plataforma Tecnológica Española Medicamentos Innovadores cuenta con apoyo financiero del Ministerio de Ciencia, Innovación y Universidades a través de la Agencia Estatal de Investigación

SPHERIUM BIOMED

PROFILE

Spherium is a company that develops biomedical innovations from academic sources to accelerate their transition to the value chain and to the market. We look for innovation opportunities both in universities and in research institutions. After thorough analysis and planning, we conduct the key activities and experiments to achieve the next value milestone. We look for the optimal partner (VC, Pharma…) to keep the project in track towards its next milestone.

SPEAKER

Luís Ruíz, CEO, Molecular biologist by training, with experience in academic research, pharmaceutical drug development and biotech start-up creation and management.

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PRODUCT

Cyclatop: Topical cyclosporine for atopic dermatitis and psoriasis

MECHANISM OF ACTION

Cyclosporine is a well-known pharmaceutical product, but it has never been successfully formulated for a topic administration.

- In Vivo data: Proven dose-dependent efficacy in animal model of atopic dermatitis Effect comparable to current gold standard topical treatment
- Safety data: Drug already approved in the indication for systemic administration

  Good in vitro skin penetration

  Minimal systemic exposure due to topical administration (GLP)

  No dermal sensitization (Buehler test in guinea pig) (GLP)

  Good tolerance in 4 Week dermal tolerance study in minipigs (GLP)

TARGET INDICATIONS

1. Treatment of Mild, Moderate and Severe Atopic Dermatitis
2. Prevention of flare-ups of the disease
3. Potential upside Psoriasis

Target Population: >2 years-old

Efficacy: Similar to Protopic, better than Eucrisa

Safety: Better tolerated than Protopic and Elidel

Minimal systemic absorption: exposure at least 100 fold lower than therapeutic dose of Neoral

Posology: Twice daily

Formulation: Scalable and stable

CURRENT STATUS

Clinical development: Phase II PoC completed

- Cyclatop improves clinical signs in mild to moderate atopic dermatitis patients assessed with EASI, ADSI and IGA scales, this improvement being significantly superior to vehicle after a 4-week treatment.
- The differential effect is observed already after 1 week
- 65% of the patients reduce their IGA score to 0 or 1 (normalization of skin condition)
- The product reduces pruritus in 3 points in a VAS scale from 0 to 10, in those patients whose basal level is superior to 4 (clinical relevant threshold)
- The results are robust, observed in both populations analyzed (ITT and PP)

CMC

- Several formulations produced within the patents scope & with regulatory compliant pharmaceutical ingredients
- Selected formulation used in preclinical and clinical studies is a sprayable emulsion
- 5% CsA. Industrial scale-up done (Sweden). 3x12 kg GMP batches manufactured
- 24 months stable formulations (25°C /60 %)

INNOVATIVE ASPECTS

- Cyclosporine is a stablished pharmaceutical product with a demonstrated efficacy in the condition. The adverse effects in the oral/systemic administration prevent a wide use of the drug
- A topical formulation, with null systemic absorption and demonstrated efficacy will be well accepted by dermatologists.
- The formulation is differential with respect to immediate competitors (Protopic and Elidel). Itching and burning at the moment of application are side effects of the competitors that Cyclatop may avoid, thus increasing treatment adherence.
- Easier to use than creams and ointments.

IPR

The project is protected by 4 patent families: Patent filing claiming the general formulation system: Priority April 15h 2011; Patent filing claiming the candidate Cyclosporine formulation space:Priority January 4th 2016; Defensive Patents filings claiming alternative Cyclosporine; and Placebo formulation space: Priority June 28th 2017.

PARTNERING OPPORTUNITIES

We are seeking for a partner specialized in the dermatology area that can continue later with the development and commercialization. We are also open to a co-development in exchange for sharing future benefits from third parties, or in territorial agreements.

IDIVAL

PROFILE

Within Valdecilla Hospital, in Cantabria, this research group at IDIVAL has two main research topics: (1) Design Listeria based nanovaccines as immunotherapies for solid tumours and (2) Prepare Listeria based vaccines for prevention of infectious diseases as listeriosis, tuberculosis or pneumonia, caused by intracellular bacteria.

SPEAKER

Dr. Alvarez-Dominguez has a PhD in Bioch. & Mol. Biol. (UAM, Madrid, 1993). She worked as Research Associate at Washington University (Saint Louis, MO, USA, 1994-99) and Centro de Biología Molecular "Severo Ochoa" (Madrid, 1999-01). She obtained the Ramon y Cajal award (2001-06, HUMV) and a tenure-track position as Research Faculty at Instituto de Investigación Marques de Valdecilla (IDIVAL, 2006-current)..

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PRODUCT

Listeria based nanovaccines as immunotherapies for solid tumours.

MECHANISM OF ACTION

Gold nanoparticles coupled by covalent chemical linkages to two ligands, β-D-glucose and a short peptide 91-99 of the bacterial toxin listeriolysin O (GNP-LLO91-99 nanovaccines). The size of the nanoparticles is 2 nm and they have homogeneous distribution on size and shape. They are non-toxic and confer stability to the two ligands, especially enzymatic stability to the peptide.

These GNP-LLO91-99 nanovaccines target to dendritic cells and cause their activation to induce immunogenic melanoma apoptosis and regression. They also activate the cytotoxic anti-melanoma immune response, expanding the cytotoxic T cells and blocking the regulatory T cells that restrict the immune responses in the tumours. These two concerted actions increase 99% the overall and long-lasting disease-free survival. They also combine and potentiate the action of other immunotherapies such as anti-CTLA-4 and anti-PD-1 checkpoint inhibitors.

TARGET INDICATIONS

Therapeutic area covering our product are oncology, oncoimmunology and dermatology. Our product can also be an adjuvant to activate the immune system serving for primary tumours as well as an anti-neoplastic product for solid metastatic tumours as a novel immunotherapy

CURRENT STATUS

- Proof of concept were performed in vivo using mice transplanted with melanoma and verified their directionality to dendritic cells and tumours.
- As monotherapies, they promoted 98% tumour regression by immunogenic apoptosis and activation of dendritic cells and enhanced 100% overall survival.
- These nanovaccines also expanded tumour specific cytotoxic T cells. As combinatory therapies, they improved the action of anti-CTLA-4 and anti-PD-1 antibodies, achieving complete remission and 100% long-lasting survival.

- As adjuvants, they activated dendritic cells in vivo using mice transplanted with tumours and in vitro using monocyte derived dendritic cells from patients with primary and metastatic melanoma. These nanovaccines activated dendritic cells from patients induced 50-60% apoptosis of allogenic human melanoma cell lines.

INNOVATIVE ASPECTS

- The main aspects compare to other immunotherapies is their double edge action, as adjuvants potentiating the onset on the immune system by activating the dendritic cells and as cytotoxic effectors on melanoma and other solid tumours causing their complete regression and the expansion of anti-melanoma cytotoxic activities deactivating the negative T cell regulators.
- But more significantly, their clear benefit in survival. An added value is their absence of toxicity and ability to combine with other immunotherapies, potentiating their effects to achieve complete tumour regression and long lasting survival. Positive results were observed in NSCLC and melanoma and possible in other tumours.

IPR

A patent application has been submitted to the OEPM (P201600160) on 24/02/2016. At the end of the priority year, we have internationally extended this application with a PCT treaty (PCT/ES2017/070103), naming as ISA to the EPO. We have received a positive IPER, that the evaluator recognized the novelty and innovation activity of all our claims, presented originally. Currently, after entry in national phases, the application is on tramit to the EPO and USPTO.

PARTNERING OPPORTUNITIES

We need a partner that invest in the product development to perform a Phase I clinical assay.

ENTRECHEM

PROFILE

EntreChem SL is the only company in the world leveraging the power of synthetic biology and combinatorial biosynthesis with drug candidates close to clinical trials. EntreChem SL brings the promise of "polypharmacology in a single drug" closer to clinical realization, since our drugs address multiple targets and pathways, both in tumor and cancer stem cells.
Drug candidates: EC-70124: next-generation Midostaurin for AML with superior metabolic and PPB profile. EC-8042: novel in class transcription reprogramming agent for tumors with genomic instability..

SPEAKER

Francisco Morís, Ph.D. in Organic Chemistry from the University of Oviedo and postdoct in The Scripps Research Institute in La Jolla (USA), worked in small US biotech companies as well as at Bristol-Myers Squibb before he co-founded EntreChem in 2005. Francisco is co-author of over 50 scientific international publications, co-inventor in over 15 patents and has raised more than 8MEUR to date from local Business Angels, Family Offices and Public.

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PRODUCT

EC-70124, multi-kinase inhibitor.

MECHANISM OF ACTION

EC-70124 potently inhibits wild-type and mutant FLT3, and also other important kinases such as PIM kinases. EC-70124 inhibits proliferation of AML cell lines, inducing cell-cycle arrest and apoptosis. EC-70124 is orally bioavailable and displays higher metabolic stability and lower human protein plasma binding compared with Novartis Rydapt®. Both in vitro and in vivo pharmacodynamic analyses demonstrate inhibition of FLT3-STAT5, AktmTOR-S6, and PIM-BAD pathways. Oral administration of EC-70124 in FLT3-ITD xenograft models demonstrates high efficacy, reaching complete tumor regression. Ex vivo, EC-70124 impaired cell viability in leukemic blasts, especially from FLT3-ITD patients.

TARGET INDICATIONS

Main therapeutic area: **Acute Myeloid Leukemia**, the drug behaves as a dual FLT3-PIM inhibitor.

Additional indications: Prostate cancer: dual NF-kB STAT3 inhibitor in both tumor and cancer stem cells; Glioblastoma: differentiation of initiating cells into senescence by NF-kB blockade; TNBC: inhibition of PI3K/mTor and JAK/STAT pathways. Combines well with docetaxel; Colon cancer: inhibition of c-scr/mTor pathways.

CURRENT STATUS

The main recent milestones consist in:

- Industrialization of the supply (recombinant strain fermentation up to 7000L, downstream processing and crystallization).

- PoC in animal models of human AML and prostate tumors, oral administration.
- Selection of murine and non-murine models for oral dosing toxicology.
- Execution of the 2-week toxicology studies (Dose Range Finding).
- Protein plasma binding functional assays

Pending to enter FIH trials:

- 28-days toxicology studies in the murine and non-murine species.
- GMP production following the industrialization protocol.

INNOVATIVE ASPECTS

- EC-70124 is a next-generation, best in class Midostaurin analog, potent and selective oral kinase inhibitor with unique activity profile, especially for AML (dual FLT3-PIM inhibitor). Other targets potently inhibited include Aurora, CHEK1, JAK and SYK. Aside from its distinct kinase inhibition profile, it shows superior metabolic stability and significantly better human protein plasma binding than Midostaurin.
- AML pipeline is heavily crowded, mostly with single target drugs. Midostaurin (Novartis Rydapt®) recent approval represents a major impact in the treatment of AML, despite the fact that it is a multikinase inhibitor, therefore considered a "dirty drug".
- EC-70124 from the same chemical family and differentiation comes from higher potency on AML targets, higher metabolic stability, and especially, 4 times lower protein plasma binding, which opens the potential to treat not only AML but also solid tumors given the significantly higher free-plasma levels if at least similar total plasma levels as midostaurin would be achieved in humans.

IPR

US: patent awarded (US 8,598,132) as filed, protecting composition of matter of a Markush formula covering a wide range of analogs including the candidate. EU: Examination in progress. No other territories covered.

PARTNERING OPPORTUNITIES

Co-development until PoC in humans in exchange of an upfront fee. From PoC until approval Entrechem won´t be involved in clinical development (only in CMC if needed), and will be compensated by advanced clinical development milestones and royalties.

ABILITY PHARMA

PROFILE

AbilityPharma is a clinical-stage biopharmaceutical company focused on developing first-in-class causing autophagy molecules through binding to the nuclear receptors PPARa/γ. It represents a novel approach, offering an opportunity to create important new therapeutic options for cancer patients. The first drug candidate ABTL0812 is currently in phase 2 clinical trials as first-line therapy for endometrial cancer and for squamous NSCLC in combination therapy in Spain and France.

SPEAKER

Albert Marofà, Business Development and Licensing Manager. Albert holds a bachelor degree in pharmacy from the University of Barcelona (2007 - 2012), and a master's degree in Bioentrepreneurship at the Karolinska Institutet (Stockholm, Sweden). Before joining Ability Pharmaceuticals, he worked at Thomson Reuters, as a Market Analyst in the Portfolio and Licensing Department. Albert Marofà supports BD&L objectives for out-licensing as well as alliance management and fund raising activities.

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PRODUCT

ABTL0812: first-in-class fully differentiated oral targeted anticancer compound causing cell death by autophagy

MECHANISM OF ACTION

ABTL0812 cause the cancer cell death by autophagy through binding to the nuclear receptors PPARa/γ. It induces TRIB3 overexpression which blocks Akt activation, the central kinase of the PI3K/Akt/mTOR pathway, thus blocking this pathway, and induces PPAR-dependent Endoplasmic Reticular Stress (ER-stress). The combination of TRIB3-mediated inhibition of the PI3K/Akt/mTOR pathway and the ER-Stress induction results in autophagy-mediated cancer cell death.

TARGET INDICATIONS

ABTL0812 has demonstrated activity as single agent and in combination in many cancer types. **The drug is currently in phase 2** for endometrial cancer and squamous non-small cell lung cancer, as first line therapy in combination with chemotherapy, followed by monotherapy chronically, and it has potential in other cancers such as pancreatic cancer, neuroblastoma, biliary tract cancer, glioblastoma, among others.

CURRENT STATUS

In the first in human phase 1/1b clinical trial (29 patients with advanced solid tumors), **ABTL0812 showed the best safety and tolerability** compared to other PI3K/Akt/mTOR pathway inhibitors. 5 patients had long term-disease stabilizations. Due to its extremely low toxicity, the recommended phase 2 dose (RP2D) was determined by PK/PD, without reaching any dose limiting toxicity. Now AbilityPharma is conducting **the phase 1/2a clinical trial (80 patients)** with ABTL0812 (at RP2D) as first-line therapy in endometrial cancer and in squamous NSCLC in combination with paclitaxel and carboplatin, the standard first-line regime. After the chemotherapy cycles, the patients remain treated with ABTL0812 chronically. The clinical trial includes leading institutions in Spain and France.

INNOVATIVE ASPECTS

- ABTL0812 is a first-in-class fully differentiated oral targeted anticancer compound causing cell death by autophagy.
- In animal cancer models ABTL0812 is efficacious as single agent with an excellent safety profile in a broad spectrum of cancer types: lung, endometrial and pancreatic cancer and neuroblastoma. In these models, the compound has also synergistic effect with chemotherapy (taxanes, platinum compounds and gemcitabine) without increasing its toxicity.
- ABTL0812 is also active on cells resistant to other targeted therapies, on tumor stem cells and inhibits metastasis formation.

IPR

Patent protection until 2030 in key territories worldwide. Licensing agreement for the development and commercialization of ABTL0812 with SciClone Pharmaceuticals for China, Hong Kong, Macao, Taiwan and Vietnam.

PARTNERING OPPORTUNITIES

We signed a licensing agreement for the development and commercialization of ABTL0812 with SciClone Pharmaceuticals for China, Hong Kong, Macao, Taiwán y Vietnam.

Currently we are looking for licensing agreements for selected territories (Russia/CIS, LATAM, Japan) or a global license with a Big Pharma.

IMIBIC

PROFILE

IMIBIC MAIMONIDES BIOMEDICAL RESEARCH INSTITUTE OF CORDOBA

UNIVERSIDAD D CÓRDOBA

The "**GC27 OncObesity and Metabolism**" group investigates the cellular and molecular mechanisms underlying the physiological regulation neuroendocrine-metabolic processes and their dysfunctions in tumor pathologies and cancer. Special emphasis is dedicated to the role played by key neuropeptide-receptor systems and their receptors, and to emerging molecular regulatory mechanisms in cancer such as alternative splicing. The group has developed a Research Area focused on the analysis of extracellular signals receptors and signaling pathways involved in the pathological interaction between metabolic dysregulations (e.g. obesity, diabetes, etc.) and the development and progression of different cancer types

SPEAKER

Dr. Raúl Miguel Luque has a vast experience in the study of the pathophysiology of endocrine-related tumors, including prostate cancer (PCa) and has made significant contributions to the fields of cellular and molecular oncology and endocrinology and metabolism. Indeed, he has published numerous research articles and reviews in the journals of highest impact of these areas [i.e. EBioMedicine, Oncogene, Mol Cancer, JCEM, Faseb J, Carcinogenesis, Cancer Letters, etc.] and has delivered multitude of invited lectures in National and International conferences.

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PRODUCT

GOAT (Ghrelin-O-aciltransferase), a new urine biomarker for prostate cancer screening

MECHANISM OF ACTION

Ghrelin-O-acyltransferase (GOAT) is the key enzyme regulating ghrelin activity by adding a unique octanoyl group to its Ser-3, and has been proposed as a potential therapeutic target for obesity/diabetes and as a biomarker in some endocrine-related cancers. However, GOAT presence and putative role in prostate cancer (PCa) was largely unknown. Our group has demonstrated that GOAT is overexpressed (at mRNA and protein level) in PCa tissues and in plasma and urine samples of PCa patients, compared with matched controls [healthy prostate tissues and plasma and urine samples from matched controls, respectively]. Through a series of subsequent studies, we have demonstrated that GOAT is consistently released to the plasma and urine of PCa patients, wherein it can be used as robust diagnostic biomarker for PCa.

TARGET INDICATIONS

The product belongs to the prostate cancer (PCa) screening area, and the final goal is to complement and/or substitute PSA as the gold standard molecule to diagnose PCa. Our data indicate that GOAT outperforms the predictive capacity of PSA as diagnostic marker and that the sensitivity of GOAT levels improves significantly when considering the patients within the so-called PSA grey-zone, a range of PSA values wherein the predictive capacity of PSA is virtually absent. Among these patients, our data indicate that the measurement of GOAT levels might represents a much more reliable biomarker for PCa screening than PSA, avoiding a high number of unnecessary biopsies.

CURRENT STATUS

- Initially, the utility of GOAT as prostate cancer (PCa) diagnostic biomarker was tested in a cohort 113 of samples of urine and plasma from control and PCa patients. These initial results have been confirmed and validated in an ample/more representative patients cohort (n~1000), which also suggest that GOAT levels could be also used as prognostic tools.
- This capacity of GOAT has been presented to several companies, which have shown high interest.
- The most recent and great milestone achievement was the admission of the technology and the group in the Caixa Impulse program, which allowed the team to valorize the biomarker.
- The program also provides a clearer business vision through mentoring activities. Moreover, the group has also obtained funding support from FIPSE to develop a business plan and a market study and from the Carlos III Health Institute [Desarrollo Tecnológico en Salud (DTS)] in order to develop a new assay to improve the performance of the asset and obtain the CE mark.

INNOVATIVE ASPECTS

- The gold standard for prostate cancer (PCa) screening is PSA. However, PSA has many limitations including its low sensitivity values (which lead to a high rate of false negatives), but also other non-cancerous events can be accompanied by high PSA levels (which also lead to a high rate of false positives).
- Other biomarkers previously proposed also have important limitations. Thus, GOAT enzyme overcomes current limitations exhibiting higher sensitivity and specificity values to discriminate PCa. For example PCA3, which was proposed as the most prominent non-PSA-based biomarker, has even reduced sensitivity. Also, other marketed test such as 4KScore relies also on PSA determination and SelectMDx has not been able to overcome all current screening limitations. Importantly, GOAT has also potential as a prognostic biomarker.
- We have demonstrated that GOAT enzyme can be used as a valuable asset for the screening of prostate cancer (PCa). Specifically, we originally found that GOAT was significantly overexpressed and secreted in PCa samples/cells and that could be detected in non-invasive samples (blood and urine) from PCa patients using a limited cohort of patients (Hormaechea-Agulla et al. Cancer Lett. 2015).
- Then, the group started to validate the capacity of this molecule in PCa screening using a more ample cohort of patients (n>300) which confirmed the capacity of GOAT as a promising PCa biomarkers, especially among patients within the "grey zone" (3-10ng/ml; Gomez-Gomez et al. J Cell Mol Med. 2018). More recently, we have complemented and validated these results demonstrating that urine GOAT levels can outperforms the predictive capacity of PSA as a diagnostic biomarker in a cohort of aprox 1000 patients and that could be used also as a prognostic biomarker.

IPR

The national patent was submitted the November 27th of 2015 and the extension to PCT was submitted the November 28th of 2016. The entrance to national phases in Europe, USA, Brazil, and other relevant countries was achieved on May of 2018.

PARTNERING OPPORTUNITIES

The group suggests a collaboration in the asset technological and regulatory development, and/or signing a license agreement with the industry.

AROMICS

PROFILE

Aromics is a biotechnology company founded in 2005 with fully operative laboratory facilities at the Barcelona Science Park and focused on developing novel therapies for the treatment of cancer and infectious diseases. Over the past five years, the company has been working in a new class of antitumor agents based on a pioneering mechanism of action: silencing aberrantly expressed proteins in poorly responsive and aggressive cancers. A focused discovery & preclinical program that has rendered a new family of chemical entities that are advancing up to clinics.

SPEAKER

Dr. Carmen Plasencia is Chemist and biochemistry specialist (BsC), PhD in Medicine (specialized in Medical Oncology), Master in Biotechnology and Master on Business Administration. More than 20 years' experience working first, at the Laboratory of Molecular Oncology (Oncology Department, Hospital Germans Trias I Pujol, Barcelona, SPAIN) where she developed her doctoral thesis and later on, occupying different positions as research associate at the Pharmaceutical Sciences Department of the USC/Norris Cancer Center (Los Angeles, California), and Private research and Technology Centers in Spain. In 2005, she co-founded AROMICS, being currently the CEO of the company. Dr. Plasencia is also co-founder and member of the board of several other small companies in Spain (Acceleromics), Italy (Aesis Therapeutics) and Boston (Acceleration Biopharmaceuticals Inc) and has extensive start-up experience on development strategy and partnering strategy both in the USA and in Europe.

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PRODUCT

NAX035: A Berberine derivative for the treatment of cancer.

MECHANISM OF ACTION

NAX035 is a first lead of new class of antitumor agents based on a pioneering mechanism of action: small molecules binding RNA, blocking the translation into protein from RNA, and thus, silencing aberrantly expressed proteins related to poorly responsive and aggressive cancers.

TARGET INDICATIONS

NAX035 is particularly effective against **malignant mesothelioma** (MM), a very aggressive, hard-to-treat and rare oncology condition that affects the mesothelium, which is the protective lining around important organs such as the lungs, the heart or the peritoneum cavity. Additional indications include lung, colorectal, refractory ovarian and pancreatic cancers.

CURRENT STATUS

- The current stage of development resulted in preclinical data which was compiled and presented to EMA regulatory agency in a first pre-submission indication meeting (November 2017), where **orphan designation** and clinical readiness aspects were discussed.
- Current activities are focused on completing regulatory package and pulling up the

product up to the first clinical trial to test safety and efficacy for MM patients.

INNOVATIVE ASPECTS

- NAX035 is a small molecule with a novel, selective and targeted mechanism of action, high anticancer potency proven in vitro and in vivo, appropriate preliminary pharmacology and safety profile, scalability potential and a simple and well-defined manufacturing route.
- Targeting Thymidylate Synthase (TS), a well defined and clinically validated target in mesothelioma responsible of the progression and the patients resistance to the current therapy.
- Innovative, targeted and selective mechanism of action by direct RNA binding molecule abolishing the aberrant expression of TS in the tumour, representing and an alternative for refractory mesothelioma patients.
- A small compound that poses some pharmaceutical advantages as stability, oral dosage, and avoidance of undesired immunogenic effects but also implying a simpler manufacturing route that supposes a lower manufacturing costs as compared to biologicals and immunological drugs currently tested in the tumor.

IPR

The family of compounds is already protected under granted patents in US, Europe and Japan.

PARTNERING OPPORTUNITIES

Aromics focuses now on moving its inventive finding up to **clinical stages** (first in man). We are looking to establish a collaboration with a big pharmaceutical partner interested in the area and with capacity to perform later and more expensive clinical trials (newer phase II/ Phase III clinical trials) and with market penetration and commercial experience to bring the product to market.

TETRANEURON

PROFILE

Tetraneuron develops a disruptive therapy against AD, based on a patent from Dr. Frade's Research Group. His Group has demonstrated that cell cycle reactivation in neurons and neuronal tetraploidization (NT) due to Thr phosphorylation of the transcription factor E2F4 participates in the etiopathology of this disease, which would be explained in oncogenic terms. Tetraneuron has a therapeutic tool whose effectiveness has already been demonstrated in animal models.

SPEAKER

José María Frade holds a PhD from the Autonomous University of Madrid. From 1996 to 1998 he worked at the Max-Planck Institute of Neurobiology. Currently, he leads a Research Group at the Cajal Institute (CSIC). He has patented the blockade of E2F4 phosphorylation in two conserved Thr residues as a therapy for Alzheimer's disease (AD), a patent that has been licensed by Tetraneuron, S.L. (Tetraneuron), a spin-off biotech company of his Laboratory.

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PRODUCT

Adeno-associated vector E2F4DN (AAV-E2F4DN) for gene therapy in neurons.

MECHANISM OF ACTION

The product is a self-complementary AAV with neuronal tropism that expresses a dominant negative form of E2F4 (E2F4DN), which is unable to become phosphorylated in two Thr residues required for cell cycle reactivation in neurons and NT.

This vector crosses the blood-brain barrier (BBB) and transduces 60-65% of brain neurons, including cortical and hippocampal neurons, which are affected in AD (Alzheimer's disease).

E2F4DN remains in the neurons for a prolonged period without causing side effects, preventing NT and working memory deficit as well as body weight loss, and improving survival in a murine model of AD.

In addition, E2F4DN increases the expression of genes that facilitate vascular integrity, the non-cytotoxic inflammatory response through DAM cells (disease-associated microglia), and reduces markers of glycophagy and autophagy, suggesting that it facilitates "brain well-being".

Therefore, gene therapy based on E2F4DN represents a promising approach for the treatment of AD as it has the capacity to prevent most of the putative etiological mechanisms of AD.

TARGET INDICATIONS

Therapeutic area of application of the product: Neurosciences. The product is indicated to prevent the development and progression of Alzheimer's disease, both in asymptomatic and prodromal stages, or even in more advanced stages of the disease.

CURRENT STATUS

- We have shown that cortical neurons from Alzheimer's Disease patients and APP/PS1 or 5xFAD mice contain phosphorylated E2F4 in Thr residues. Neuronal expression of the

E2F4DN transgene blocks NT and reverses the loss of body weight and cognitive deficits observed in 5xFAD mice.

- In addition, it triggers the activation of the transcriptional program that promotes neuronal survival, axonal regeneration and synaptic plasticity, enhances memory and prevents cognitive loss in a murine model of AD.
- The systemic administration of an adeno-associated vector with neural tropism and capable of crossing the BBB, expressing E2F4DN in neurons also blocks NT, increases survival and reverses the loss of body weight and cognitive deficits observed in 5xFAD mice.
- This therapeutic vector has no deleterious effects, does not induce tumors and, despite being detected in the liver and spleen, does not cause hepatic or hematological alterations..

INNOVATIVE ASPECTS

- AD is a pathology of multifactorial etiology, currently lacking an effective therapy. For decades, most therapies have focused on the amyloid hypothesis, but several clinical trials based on the elimination of senile plaques have been unsuccessful. Other therapies in development focus on specific aspects of the pathology (eg reduce inflammation, limit vascular alterations, enhance neuroprotection, etc.).
- In contrast, our therapy is multifactorial since prevention of E2F4 phosphorylation facilitates the key role of this transcription factor in quiescence and favors a gene program that enhances cerebral homeostasis, which is known to be altered in AD.

IPR

We have a patent entitled "Phosphorylation on the Thr-248 and/or Thr-250 residues of transcription factor E2F4 as a therapeutic target in pathological processes associated with somatic polyploidy" granted in the EU (EU Patent No. 2783696), USA (US9567384B2) and Japan (JP6100276B2).

PARTNERING OPPORTUNITIES

Our focus of Collaboration (more than cooperation) would be in the line of securing options or license agreements in case the research is having the expected results. We expect this collaboration would allow us to advance quicker, with the pharma support and know-how in order to reach our common goal.

IGTP

PROFILE

The Institute for Health Science Research Germans Trias i Pujol (IGTP) is a public research centre in the Autonomous region of Catalonia in Northern Spain dedicated to increasing scientific knowledge and transferring it to improve the care and lives of patients. Among others, the identification of diagnostic biomarkers for dementia with Lewy bodies is one of the main objectives of the GTS-group.

SPEAKER

Katrin Beyer, PhD, Principal investigator. Katrin leads the group of Genomics and Transcriptomics of synucleinopathies (GTS group) in the Department of Pathology of the Germans Trias i Pujol Research Institute in Badalona (Barcelona, Spain). She has worked in the molecular characterization of dementia with Lewy bodies indentifying overlaps and differences with related diseases such as Parkinson's and Alzheimer's disease for 15 years.

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PRODUCT

Diagnostic biomarker for the differential diagnosis of dementia with Lewy bodies

MECHANISM OF ACTION

We offer a peripheral biomarker panel composed of a group of alpha-synuclein mRNA transcripts and a platelet-derived miRNA. Their determination will be carried out in whole blood samples of an individual. Whereas alpha-synuclein transcript expression levels correlate with the alpha-synuclein aggregation rate in the brain, platelet-derived miRNA-XXX expression differentiates between DLB and Alzheimer's disease (AD) with sensitivity and specificity of more than 96%.

TARGET INDICATIONS

The intended use of the biomarker at its present state of development is the correct identification of patients with dementia with Lewy bodies (DLB), especially to differentiate them from Alzheimer's disease. This correct differentiation will improve the application of therapies on one hand, and on the other it will enable more efficient clinical trials by allowing accurate identification of patients who may benefit from the therapeutic intervention under study.

CURRENT STATUS

- *Alpha-synuclein mRNA transcripts*: We have carried out three validation studies and included a **total of 91 DLB patients and 48 control subjects**. DLB were divided in dependence on the disease duration and patients who developed DLB recently showed an important diminution of 3 SNCA transcripts. SNCAtv3 expression correlated with disease progression. Its levels are most diminished at early, and normal at advanced stages.
- *Platelet derived miRNA-XXX*: Expression levels were analyzed in 4 independent DLB/control cohorts with a **total number of 33 DLB patients and 37 control subjects**. As an additional validation, we carried out a blind study including also samples of Alzheimer patients. Sensitivity and specificity to differentiate between DLB and controls was of 87% and between DLB and controls of 96%.

INNOVATIVE ASPECTS

- At this moment, peripheral molecular biomarkers either for the clinical diagnosis of DLB or for the differentiation between DLB and AD do not exist. The clinical diagnosis of DLB is based on clinical signs and DaTScan, an expensive and invasive SPECT imaging technique using a radiopharmaceutical agent.
- Instead we aim to provide a biomarker easy to obtain and to determine.
- We expect that this biomarker will also allow the early diagnosis of DLB within a group of individuals of risk.

IPR

We have requested two patents for the protection of our biomarkers: (1) EP15382241.6 with the TITLE: Method for in vitro diagnosis of synucleinopathies using a-synuclein gene transcripts, and (2) EP18382540.5 with the TITLE: In vitro method for the diagnosis of synucleinopathies.

PARTNERING OPPORTUNITIES

- Co-development
- Licensing Out
- Offering services for patient stratification.

ANKAR PHARMA

PROFILE

Ankar Pharma is a spin-off biotechnological company focused on the discovery and development of innovative drugs for unmet neurological disorders including neurodegenerative diseases.

SPEAKER

Ana Martinez, PhD, is a research professor at CSIC, where she is head of translational medicinal and biological laboratory at CIB-CSIC. From 2002 to 2008, R&D director of NeuroPharma where two compounds were developed to enter in clinical trials. She is founder of ANKAR Pharma, scientific advisor of several biotechs and currently, she has five patents under development by three different companies

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PRODUCT

AP-1, a remyelinating small molecule drug for the oral treatment of multiple sclerosis.

MECHANISM OF ACTION

AP-1 is able to modulate allosterically two important targets expressed both in central nervous system and in peripheral blood cells with synergic effects.

Through this innovative pathway that involves a serine/threonine kinase and a specific cAMP phosphodiesterase, AP-1 is able to decrease neuroinflammation, macrophage infiltration in brain and promotes remyelination in different in vitro, ex vivo and in vivo paradigms.

TARGET INDICATIONS

The preclinical proof-of-concept has been done in 3 independent models of **multiple sclerosis**. A second indication for retiniosis pigmentosa has been preclinical proved. The mechanism of action support the use of AP-1 for other neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.

CURRENT STATUS

- Chemical, pharmaceutical and toxicological preclinical development to reach clinical phase I studies are ongoing. The IMPD will be ready for regulatory agency submission at the end of 2019.
- Main preclinical results are: 1) AP-1 is effective in decrease the neurological score in a EAE model both when it is administered in the onset or in the peak of the disease; 2) AP-1 increase corpus callosum remyelination in a cuprizone mouse model; 3) AP-1 increase axon diameter in a lysolecithin demyelination model; 4) AP-1 promotes human and murine OPC differentiation in vitro; and 5) The PK profile of AP-1 is compatible with an oral administration.

INNOVATIVE ASPECTS

- AP-1 is a small heterocyclic molecule that has an excellent profile for multiple sclerosis treatment.
- In different preclinical studies, AP-1 has shown neuroprotective, anti-inflammatory and

potent remyelinating profile having an innovative mechanism of action.

- Differentiation of human OPCs is increased with AP-1 treatment. OCT has been shown to be a good technique for in vivo remyelination evaluation after AP-1 administration in a preclinical assay.
- The compound has started chemical regulatory development. It is a safe small molecule that can be orally administered.

IPR

AP-1, together with more than 15 different related derivatives, is protected by a compound patent granted in USA, Australia, Europe (extended to 8 countries), and it is in prosecution in Canada.

PARTNERING OPPORTUNITIES

We are looking for pharmaceutical partners to co-develop AP-1. First option agreements are also seeked.