MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

XXII Encuentro de Cooperación Farma-Biotech

Martes, 15 de noviembre de 2022

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 22 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.

La jornada tendrá lugar **de forma presencial** en la sede de Farmaindustria en Madrid.

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

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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	*Nuevo fármaco neuroprotector para tratamiento del ictus.*	Ensayos preclínicos	***Youness Ouahid*** ISQUAEMIA BIOTECH
10:15 10:45	*Aptámero contra el cáncer de mama.*	Ensayos preclínicos	***Miguel Moreno*** APTUS BIOTECH
10:45 11:15	*Nueva entidad química para retinosis pigmentaria*	Ensayos preclínicos	***Pablo Ferrón*** MIRAMOON PHARMA
11:15 11:45	*Terapia contra la distrofia miotónica tipo 1*	Preclínica Regulatoria	***Pedro Fernández Nohales*** ARTHEX BIOTECH
	DESCANSO. Café y refrescos. Contactos informales		
12:00 12:30	*Biomarcador para la detección temprana de sepsis*	Probado en 200 pacientes	***Enrique Hernández*** LOOP DIAGNOSTIC
12:30 13:00	*Generación de tolerancia antígena específica para patologías autoinmunes*	Preclínica Regulatoria	***Marti Dalmases*** AHEAD THERAPEUTICS
13:00 13:30	*Ciclina M4 como nueva diana contra enfermedades hepáticas*	Ensayos preclínicos	***Mª Luz Martínez Chantar*** BIOGUNE
13:30 14:00	*Modulador metabólico para enfermedades inflamatorias*	Ensayos preclínicos	***Josep Mª Aran*** IDIBELL
	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 15 de noviembre de 2022.**

MINISTERIO DE CIENCIA E INNOVACIÓN
AGENCIA ESTATAL DE INVESTIGACIÓN

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PRESENTACIONES QUE TENDRÁN LUGAR EN ESTA JORNADA

PROFILE

Isquaemia Biotech is a biopharmaceutical company that develops new compounds for highly prevalent and currently untreated diseases, mainly related to neurovascular pathologies, with a first line of development in central nervous system and especially in acute ischemic stroke.

SPEAKER

Youness Ouahid, PhD in Biology from the Autonoma University of Madrid (UAM), has over 15 years of industry experience, leading high potential healthcare and biotechnology projects, assessing innovation and R&D development and transferring it to the market. He has extensive experience as an adviser, consultant and mentor for biotechnology companies and projects in the healthcare sector, both in the public and private sectors. He is an open innovation entrepreneur, R&D and TechTransfer manager, co-founder/partner of several companies.

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PRODUCT

ISQ-201: Lead compound from a new family of small molecules "steronitrones"

MECHANISM OF ACTION

ISQ-201 is a new small molecule neuroprotective drug for the treatment of Acute Ischemic Stroke (AIS). ISQ-201 significantly reduces the stroke penumbra zone and protects neurons after reperfusion from oxidative damage adjacent to oxygenation.

In short, it reduces neurological damage and therefore the comorbidity caused by this pathology, reducing disability, and increasing the quality of life of patients. The drug candidate ISQ-201 has successfully completed the GLP preclinical phase and is facing GMP regulatory phase.

ISQ-201 has neuroprotective action, activation of the cellular antioxidant response and it is an agent capable of reducing the neurological damage caused after Stroke.

ISQ-201 is a free radical scavenger drug (ROS scavenger), which limit ROS production and neuronal apoptosis. Its ANTIOXIDANT ACTIVITY is given by the nitrone structure, with scavenging activity with higher antioxidant capacity.

The mechanism of action of this drug has been validated in vitro & in vivo studies.

TARGET INDICATIONS

The primary indication for ISQ-201 is the treatment of **acute ischemic stroke** (AIS). However, ISQUAEMIA plans to expand the clinical use of ISQ-201 for other applications such as permanent ischemia. In addition, the preliminary results also indicate its potential use in other neurological pathologies, such as Amyotrophic Lateral Sclerosis.

CURRENT STATUS

- The drug candidate ISQ-201 has successfully completed the GLP preclinical phase and is about to enter the GMP regulatory phase.
- It has achieved the following milestones in vitro studies: Oxygen–Glucose Deprivation (OGD) Primary neuronal cultures; Efficacy, Toxicity & MoA.
- It has achieved the following milestones in vivo studies: Focal cerebral ischemia model; Transient global cerebral ischemia model (*improvement of long-term cognitive impairment assessed by spatial; recognition & memory test, improvement of the functional motor deficit assessed by Grip Strength test; reduction of the infarct size at 0.1 mg/kg ISQ-201 dose and with a 21-33 % the reduction in lesion size*)
- Pharmacological characterization -GLP preclinical phase: ***Toxicity*** (non-mutagenic, non-promutagenic, non-Haemolytic Activity, non-Chronic Toxicity, non-Cardiotoxicity); ***Kinetics*** (the half-life around 1.5–2h showed that ISQ-201 was eliminated quickly, Dose dependent activity with Cmax and AUC0-8h values of ISQ-201 (0.07–1.00 mg/kg) and LLOQ (1.0 ng/mL); Hematoencephalic permeability of ISQ-201 659 times more than NXY-059)

INNOVATIVE ASPECTS

- ISQ-201 has shown higher cell permeability (Blood-Brain Barrier - BBB) and neuroprotection than other drugs in development and marketed. Indeed, ISQ-201 has shown greater cell permeability (BBB) and neuroprotection than other drugs such as NYX-059 (withdrawn in Phase III), and Edaravone (in use in Japan).
- In short, ISQ- 201 has: Higher neuroprotection; Higher cell permeability; Great potential for long-term neuronal protection; Higher efficiency; Improves both neurological deficit and neuroprotection after transient ischemia.

IPR

Isquaemia's new drug is protected under several patent families:

1. PCT/ES2014/070421: Steroidal nitrones for the treatment and prevention of AIS, Alzheimer and Parkinson diseases and Amyotrophic Lateral Sclerosis.

2. PCT/EP2019/077525: Quinolylnitrones for the treatment and prevention of a cerebral stroke or ischaemia.

3. PCT/EP2021/055653: "Steroidal nitrone for the treatment and/or Prevention of a cerebral stroke or ischaemia"

PARTNERING OPPORTUNITIES

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

PROFILE

Aptusbiotech is a start-up SME founded in 2010 with a pipeline focused on researching novel therapies based on aptamer technology. Additionally, Aptusbiotech is also a service company where we make all our experience available to our clients to apply it to the development and application of aptamers in their specific applications: diagnostic, therapeutic or biotechnological. Our goal is to become a leading company in the development of new biotechnological applications based on aptamers.

SPEAKER

Miguel Moreno received his Ph.D. in 2005 at the University of Alcalá de Henares. He has an extensive academic experience across the CNB-CSIC or Centre of Astrobiology (CSIC-INTA) in Spain as well as senior research scientist at the University of East Anglia. As business entrepreneur he co-founded Bioapter and Aptatargets. In January 2020 he joined AptusBiotech as CSO where he is responsible for implementing new projects and business for the company.

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PRODUCT

A new drug based on an aptamer against Protein Kinase MNK1b

MECHANISM OF ACTION

apMNKQ2 is an aptamer targeting kinase MNK1b. Aptamers are single-stranded nucleic acids of short length in vitro selected from a large random sequence pool to bind stably and highly specific for their targets. Relatively easy and reproducible production and labelling, cost-effectiveness and stability during long-term storage, aptamers technology is an innovative alternative and much less known than that of monoclonal antibodies.

PI3K/AKT/mTOR and MAPKs pathways are interconnected and converge at MNK1. Previous results have shown that MNK1b is overexpressed in breast cancer, mainly in the triple-negative type, and that its expression correlates with a poor prognosis. Thus, pharmacological inhibitors directed against MNK seem to provide an effective anti-tumour strategy that is not harmful to non-tumour cells. apMNKQ2 aptamer has shown to inhibit tumorigenesis in three breast tumour lines; to produce cell death, mainly through an apoptotic mechanism mediated by caspase; and to inhibit the metastatic capacity of breast tumour cells.

TARGET INDICATIONS

The therapeutic area of application is Oncology, with a main indication in breast cancer, but also with outstanding results in other related indications as lung cancer, pancreas cancer and anaplastic thyroid cancer, mainly where MNK1b malfunction is correlated with tumour appearance.

CURRENT STATUS

- Non-regulatory pre-clinical studies for the treatment of breast cancer with apMNKQ2 injected intraperitoneally, with no requirement of vehiculation, have shown capable of reducing tumour size, inhibiting tumour cell proliferation and inducing apoptosis in an orthotopic model of triple-negative breast cancer in mice, with the MDA-MB-231 tumour line.

- Alongside, similar experiments with an orthotopic pancreas Patient-Derived Xenograft (PDX) model in mice is resulting in reducing tumour size in 70 % when compared with controls.

INNOVATIVE ASPECTS

- The main competitive advantage of apMNKQ2 lies in the fact that it acts in a pathway against which there are currently no clinical drugs, although there are some related phase I and II clinical trials, none of which have studied specific inhibitors of MNK1.
- On the other hand, there are several drugs that affect the PI3K/AKT/mTOR pathway already approved for clinical use, with a high number of clinical trials (more than 250 in different phases), most of which study the effect combination of these drugs.
- We have not detected any clinical trial in which the combined effect of inhibitors of both pathways is studied.
- Moreover, apMNKQ2 have shown not toxicity in mice, high stability is blood plasma and no side effects.

IPR

Patented in national phases (EP18382888.8) by IRICYS (PCT/EP2019/083547) requesting the national phase in the USA Application No. 17/299,110 (06/02/2021) and European Regional 19 809 531.7 (06/28/2021), with exclusive use license for Aptusbiotech.

PARTNERING OPPORTUNITIES

As Aptusbiotech is carrying out non-regulatory pre-clinical studies for the treatment of breast cancer, and advanced experimentation in both pancreatic cancer and anaplastic thyroid cancer, we are seeking a partner/investor/licensee to carry out the following phases of clinical trial.

PROFILE

Miramoon Pharma was founded at 2Q-2019 as a spin-off from the Basque Country University and Biodonostia Health Research Institute. Our objective is to develop small chemical entities for the treatment of orphan diseases that can be used as a steppingstone to achieve approval in major diseases.

The first program is in lead optimisation for Retinitis Pigmentosa (RP) and can be developed in diabetic retinopathy. We have other programs in lead nomination for DMD, DM1, ALS, AD and ageing.

SPEAKER

Pablo Ferrón, CEO of Miramoon Pharma, has a Master's degree in Synthetic and Industrial Chemistry. He has participated in the design and synthesis of the first MP compound. Pablo Ferrón already had business experience (in 2010, founded an industrial start-up: Gomavial Solutions) when he started leading Miramoon Pharma in 2019.

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PRODUCT

MP-004, the new standard for the treatment of Retinitis pigmentosa (RP)

MECHANISM OF ACTION

MP-004 is a NCE (small molecule) that has demonstrated efficacy in several representative animal models of Retinitis Pigmentosa through topical ocular administration, improving rods and cones' structure and function.

MP compounds are a novel isomerase protein ligand that modulates the ER channel activity preventing calcium leakage from oxidatively stressed channels under pathological conditions.

Moreover, they can act as a ROS scavenger, reducing the formation of highly reactive deleterious species.

Both mechanisms contribute to normalize the intracellular calcium homeostasis in photoreceptors, keeping the Ca2+ concentration below the levels required to trigger cell apoptosis.

Unlike gene therapy approaches, it can be effective for all RP patients and can be used concomitantly with other therapeutic strategies. It has optimized physicochemical and ADME properties. Also has demonstrated very low toxicity and high selectivity. Its manufacture is easily scalable and has a low manufacturing cost.

TARGET INDICATIONS

Retinitis pigmentosa (RP). Therapeutic treatment. RP is a group of Inherited Retinal Dystrophies (IRDs) characterized by progressive degeneration of photoreceptors or retinal pigment epithelium, leading to night blindness, tunnel vision, and gradual reduction of central vision. RP is the most common IRD.

CURRENT STATUS

- MP-004 is now ending lead optimization activities and starting the preclinical package experiments.
- We also have applied to FDA for the Orphan Drug Designation for MP-004 to treat RP.
- In mice model rd10 (the most widely used for RP)- Improved rod function (rod b-wave) by 41% compared to untreated group at p25 starting at p14, and improves Optokinetik - Water-Maze results at p30 starting at p14.
- In model rd3 (an additional model of completely different mutation)- improved rod function (rod b-wave) by 33% compared to untreated group at 2 months starting at p14.
- Both models have been treated with once a day dose administered via topical drop.
- MP-004 reaches retina after topical administration in mouse, rat, rabbit and pig in therapeutic concentration. This is a feature that makes it unique in its kind.

INNOVATIVE ASPECTS

- MP-004 can cross the blood-retinal barrier and reach the retina following non-invasive topical ocular administration.
- Compared to gene therapy, our main advantages are: 1) broad spectrum of action for most patients (compared to <1% of Luxturna); 2) avoiding invasive retinal surgery (with associated serious side effects); 3) compatibility with other therapies; 4) topical and safe application (self-treatment avoiding systemic exposure); and 5) economically affordable.

IPR

1st Patent (Priority 04/2016) Granted in EU, US, Australia, Japan, Russia, Chile and Mexico. 2nd Patent Application (Priority 06/2022) covers backup compounds and ocular diseases.

PARTNERING OPPORTUNITIES

Investment for Development of RP program. Collaboration for Development of any program. Licence of any program.

PROFILE

ARTHEx Biotech is a global leader in the development of investigational anti-microRNA (antimiR) oligonucleotide drugs for unmet diseases thanks to its proprietary ENTRY™ platform. The ENTRY™ Platform by ARTHEx Biotech allows fast and flexible development of short-length investigational oligonucleotides to treat diseases by inhibiting microRNAs in the most relevant tissues. Currently, ARTHEx is advancing its antimiR drug pipeline across 4 diseases: myotonic dystrophy (DM), which is the most advanced application, cachexia, Fuchs endothelial corneal dystrophy and osteoarthritis.

SPEAKER

Pedro Fernández, Director of Operations of Artex Biotech, holds a MSc in Biochemistry and Ph.D. from the Universitat Politècnica de València. He also holds a postgraduate degree in R&D management and is an accredited Registered Technology Transfer Professional (RTTP) by the internationally recognized ATTP. He counts on eight years of experience in technology transfer, project management, and R&D management. Prior to joining ARTHEx Pedro Fernández co-founded the company Tricopharming, which researches different biotechnological applications of trichomes in plants. At ARTHEx, he is responsible for the management of the company's scientific activities and business operations, including overseeing the Intellectual Property portfolio and strategic partnerships.

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PRODUCT

ATX-01: a first-in-class disease-modifying therapy for Myotonic dystrophy type 1 (DM1)

MECHANISM OF ACTION

ATX-01 is a disruptive drug product for DM1 that addresses myotonic dystrophy's cause in a specific, highly effective and safe way through miRNA-based therapeutics. ATX-01 consists of a 16nt long oligonucleotide conjugated to a fatty acid that allows to deliver differentially the active ingredient to the most relevant tissues (muscle, heart, brain) at low effective concentrations.

ATX-01 targets miR-23b, a miRNA that impacts the cause of the disease. DM1 is caused by abnormal CTG repeats in a non-coding region of DMPK gene. After transcription, the DMPK toxic miRNA folds into a hairpin that sequesters MBNL proteins. Long CUG repeats also produce an overexpression of miR-23b that represses MBNL protein translation. Both events produce a general loss of function of MBNL proteins, key regulators of splicing, causing the symptoms of DM1. ATX-01 blocks miR-23b, increasing MBNL protein levels and reversing the disease phenotype.

TARGET INDICATIONS

ATX-01 is a first-in-class treatment for Myotonic dystrophy type 1 (DM1). DM1 is a clinically and genetically heterogeneous neuromuscular disorder with a prevalence of 1 in 8,000 people worldwide. It is the most common adult muscular dystrophy and, currently, there is no disease-modifying treatment, but only symptomatic treatments. Previous studies show that congenital DM, Myotonic Dystrophy type 2 (DM2), among others, share similar mechanism of action, implying that ATX-01 may be effective for these diseases as well.

CURRENT STATUS

- ARTHEx identified miRNAs that directly regulate MBNL1/2 in HeLa cells and confirmed that silencing miR-23b or miR-218 increased MBNL protein levels and rescues molecular defects in DM1 myoblast.
- Then, ARTHEx assessed antimiR oligonucleotide capacity to block miR-23b or miR-218 and reach target tissues, giving as result 75% rescue of myotonia (functional rescue) and 50% of splicing rescue (molecular rescue) in a DM1 mouse model (HSLAR mice). These latest models showed normalized strength for up to 1 month after injection and MBLN1 protein levels upregulated for up to 40 days.
- The toxicology preclinical studies of ATX-01 are about to finish by the end of this year and have shown no adverse effects in the kidney nor liver at maximally tolerated doses so far. We have the ODD in US and its development plan has been approved by the FDA in a pre-IND meeting.
- Finally, the phase I/IIa clinical study in DM1 patients will start in the beginning of 2023.
- The clinical roadmap for ATX-01 has been validated by the FDA (pre-IND meeting in September 2021) and the phase I/IIa clinical trial will start in 2023. Moreover, ATX-01 has obtained Orphan Drug Designation (ODD) in the US.

INNOVATIVE ASPECTS

- ATX-01 is a unique and innovative disease modifying treatment for DM1 with a first in class mechanism of action that addresses a new target, the miR23-b, by an improved tissue delivery strategy that increases potency in muscle and brain and decreases toxicity and that has been developed by ARTHEx's own protected technology.
- ATX-01 has a first of its kind dual mechanism of action since it is the only therapy able to simultaneously target miR23b and rescue MBNL while other agents have only a single mechanism of action.
- What is more, the unique tissue delivery technology of ATX-01 allows to deliver differentially the active ingredient to the most relevant tissues (muscle, heart, brain) at very low effective concentrations while other therapies in development have not shown target engagement apart from muscle meaning that none of the other solutions have potential to treat other diseases as congenital DM or DM2.
- Regarding the scale up process, ATX-01 will reach the market in a relatively short time in comparison to its competitors since it is a product of chemical synthesis so its costs, production times and regulatory requirements are lower than other advanced therapies in development.
- Finally, the clinical development of ATX-01 is being facilitated by the fact that it has obtained Orphan Drug Designation (ODD) in the US (currently, in process at EMA). ATX-01, therefore, is uniquely positioned to offer a better solution to manage DM1, in the event that other drugs come to market.

IPR

Currently, ARTHEx's technology is protected by two patent families (WO2018050930 owned by University of Valencia and EP22382493, co-owned by University of Valencia and Arthex) that have been exclusively and globally licensed to Arthex.

The strong IP protection strategy of the company impede other entities to: A) use our fatty acid delivery platform for oligonucleotides; B) exploit Arthex's antimi-23b and antimiR-218 leads and, C) the medical use for DM of antisense oligonucleotides that inhibit miR-23b or miR-218.

As co-owners and exclusive licensees of the patents applications that protect the technology (the ENTRY™ platform, the lead antimiR-23b, its backup antimiR-218 and their medical use for DM) ARTHEx is in a privileged position up to 2042 and have freedom to operate.

PARTNERING OPPORTUNITIES

We have recently opened a series A of $40M that will allow us to complete a phase I/IIa, carry out the chronic regulatory preclinical in parallel and advance another two treatments still in the discovery phase against osteoarthritis and muscular cachexia in lung cancer. We look for a pharmaceutical company willing to co-invest in our company. On the other hand, we are also looking for partnering specialty pharma companies with expertise in cGMP manufacturing, clinical trials, and global sales and marketing to co-develop or explore licensing opportunities.

PROFILE

Loop Dx has developed a fast test for early detection of blood bacterial infections. The goal is to help ERs diagnose patients that are developing sepsis (the body's inflammatory response to a serious infection, often deadly) so they can quickly be administered intravenous antibiotics. Loop Diagnostics started in MOEBIO's dHEALTH BCN program, a disruptive talent initiative powered by Biocat and inspired by Stanford Biodesign. Founded in 2018 by PhD Enrique Hernandez with the assistance of MD in immunology and infectious diseases, Erika Plata. Loop-dx builds on research carried out by IdiBell, with the vision to develop and commercialize diagnostic solutions that allow bloodstream infections to be diagnosed early. At SeptiLoop we are developing a diagnostic device for accurate triage in the emergency department, that would rapidly identify patients without clear symptoms of sepsis. Since 2018, rapid progress has been made. Successful preclinical trials have demonstrated the effectiveness of the first product, SeptiLoop, targeting the early diagnosis of Sepsis, faster and with greater precision than the existing standard of care.

SPEAKER

Enrique Hernández Jiménez, Founder and CEO of Loop Dx. In 2017, he finished his PhD at Hospital La Paz in Madrid, analysing immune response in several diseases, including sepsis. He published more than 25 papers in 5 years but decided to pivot his career by joining the d·HEALTH Barcelona program promoted by Biocat. During the program, he did a clinical immersion at Institut Guttmann, where he came up with the idea that has led to his start-up: Loop Dx.

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PRODUCT

SeptiLoop, a novel first-in-class in-vitro Point of Care diagnostic device that identifies early bloodstream infections by detecting specific immune response biomarkers

MECHANISM OF ACTION

At Loop-dx we have focused on understanding the molecular mechanisms taking place during this refractory stage (ET phase) and using them for the diagnosis of sepsis. Our approach offers a more conclusive and broader diagnosis rather than detecting the specific pathogen in the bloodstream, since every patient undergoes the ET phase. SeptiLoop has the ability to identify the state of "endotoxin tolerance" (endotoxin tolerance, ET) caused by a bacterial infection in the bloodstream. In this way SeptiLoop get a high sensitivity (detects 86% of positives) and maximum specificity (detects 100% of negatives).

TARGET INDICATIONS

Sepsis.

CURRENT STATUS

- First functional prototype developed.
- Product design completed, validated and European patent application submitted.
- Important efforts have been done to develop and prototype of both the lateral flow and the reader technology.

- Successfully completed all pre-clinical tests with excellent results.
- Specificity validation: In this study we enrolled negative control groups consisting of healthy volunteers (HV, n = 50), non-septic patients with an inflammatory history such as cardiac surgery patients (CS, n = 50) and Septic patients (n = 100).
- The study showed a lower threshold level for the detection of the biomarkers, enhancing the specificity and sensitivity when compared with the levels of the same biomarkers in the septic population, and giving significantly higher Negative Predictive Values (NPV).

INNOVATIVE ASPECTS

- Loop-dx proposes a totally innovative approach based on detecting the specific immune response to sepsis, allowing the infection to be detected earlier and more accurately than the current diagnostic techniques.
- SeptiLoop detects biomarkers related to the patient's immune status in order to obtain an accurate, fast, and cost-effective point-of-care device for the early diagnosis of sepsis infection allowing its rapid treatment, and therefore, reducing mortality.
- Our technology identifies the initial bloodstream infection during the first hours (after 1 hour of the infection), whereas the other biomarker competitors start rising after the 6 hours of the infections; moreover, the competitors that detect pathogens start 12 hours after the initial infection.
- In addition, our diagnostic method can be detected within less than 2 hours providing actionable clinical information of suspected sepsis cases without clear symptoms (before qSOFA). In this way, clinicians can diagnose sepsis and start clinical protocols according to this condition.
- With SeptiLoop time to treatment is reduced at least 3 hours as it diagnoses sepsis in early stages and the test only takes 2 hours to give the results.

IPR

Loop-dx 's Technology is protected with a European patent application number EP20382462.8 – METHOD AND KIT FOR THE EARLY DETECTION OF SEPSIS with priority date 8/06/20. We extended the protection via a PCT application by June 2021, and plan to enter National Phases by December 2022. The technology was developed jointly with researchers of Bellvitge Hospital, and therefore it is jointly owned by Loop-dx and Idibell (Institute of Research of Bellvitge Hospital) 51% and 49% respectively. Loop-Dx has obtained a license to the ownership portion corresponding to Idibell in the framework of an exclusive, royalty bearing, perpetual, worldwide agreement. This agreement confers Loop-dx exclusive worldwide exploitation rights to the technology, including right to sublicense.

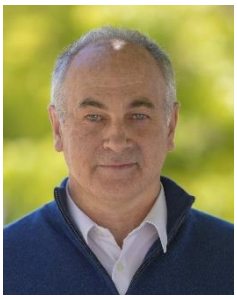
PARTNERING OPPORTUNITIES

We want to explore other uses of SeptiLoop IVD test (as companion diagnostics of other drugs or medical devices). For example, to check the status of immunosuppressed patients from chemotherapy or/and to study the immune status of patients who received immunomodulatory drugs.

PROFILE

Ahead Therapeutics is a biotechnology company founded in December 2017 to develop the technology co-invented by researchers from Germans Trias & Pujol Health Sciences Research Institute (IGTP) and the Catalan Institute of Nano Science and Nano Technology of Catalonia (ICN2). Ahead Therapeutics is going to put a breakthrough nano-tech platform on the market for treating and curing autoimmune diseases. The intellectual property covering PS-Liposomes was transferred to Ahead Therapeutics. Since then, the Company has generated efficacy results using in vivo and ex vivo models in all the indications of our pipeline (T1D, MS, RA, CD, MG, NMO, MYO) and now we are raising funds to push to clinical trials the two selected leading assets RA and MG.

SPEAKER



Dr. Martí Dalmases is the CEO of Ahead Therapeutics, He has a PhD in Medicine and a Master in business administration (UAB), as well as, a Master in Scientific Communication (UPF) and a Master in Hyperbaric Medicine (UB). Dr. Marti Dalmases has had responsibilities in different environments of the health sector: hospital management; university lecturing; consultancy at national and international level; R&D+i project management and science divulgation as a founder of "Educación Médica" scientific review. In recent years, Dr. Marti Dalmases has been very active in the technology transfer field. He was Healthcare Director at KIM, and he has founded some start-up companies, or helped them to grow, participating as a business angel (BA investor and in some cases as a member of the Board). These include SOM Biotech; TR Composites; Confirmsign; Nanosel; IDP Discovery Pharma, and Centauri Biotech.

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PRODUCT

Liposome-based Biomimetic Therapy Platform for autoimmune diseases

MECHANISM OF ACTION

In an autoimmune disease, the immune system attacks by mistake our self-tissues. This type of error causes more than one hundred autoimmune diseases that are very well described. Ahead Therapeutics technology fixes this error re-programming the immune system. It restores the original tolerance (self-tissue recognition). So, the result is that the autoimmune attack stops.

Ahead Therapeutics' approach corresponds to a new knowledge field known as "antigen-specific immune tolerance generation". Ahead's platform mimics an essential process in immunological tolerance induction, and self-tissue recognition called efferocytosis, i.e. engulfment of apoptotic cells by antigen-presenting Dendritic Cells. Our Liposomes, specifically designed to mimic apoptotic bodies, encapsulate the "specific autoantigen" (a piece of protein) responsible for activating autoimmunity (the disease). The product generates tolerance against the autoantigen, and consequently, it cures the disease.

It is a technological platform: only by changing the auto-antigen encapsulated we can address different diseases. That is, we do not have a single product but several.

TARGET INDICATIONS

Autoimmune diseases. Nowadays, development programs include Rheumatoid Arthritis, Myasthenia gravis, Type 1 Diabetes, Multiple Sclerosis, Celiac Disease, Neuromyelitis Optica and Myositis.

CURRENT STATUS

- Ahead Therapeutics was founded in December 2017 to develop the technology co-invented by researchers from IGTP and ICN2.
- In the beginning, the company corroborated previous research results in Type 1 Diabetes (T1D) and Multiple Sclerosis (MS) and contrasted the value of the tech-platform.
- After talking to KOL, Big pharma, and VCs, Ahead Therapeutics dedicated its efforts to expand the pipeline with large market (Rheumatoid Arthritis (RA), Celiac Disease (CD)) and rare/orphan indications (Myasthenia Gravis (MG), Neuromyelitis optica (NMO) and Myositis MYO), prove that Ahead's liposomes are a real technology platform.
- After obtaining excellent results in all in vivo and ex-vivo assays performed, Ahead Therapeutics has decided to focus next years on developing two leading assets RA and MG.
- Regarding CMC development, Ahead Therapeutics has a cleanroom facility where more than 500 batches have been produced to test the technology in the selected indications.
- The production process has been developed towards a scalable method, and a collaboration with the analytical chemistry group from Barcelona University has been established to develop all the analytical methods for the product's characterization.

INNOVATIVE ASPECTS

- Currently, the treatment of autoimmune diseases is only symptomatic and palliative, based on immunosuppressants with many side effects. In contrast, Ahead Therapeutics' technology based on generating antigen-specific tolerance represents two significant qualitative advantages for patients diagnosed with autoimmune diseases:
  - firstly, treatment with PS-Lipo-Ag has no known side effects and does not generate systemic immunosuppression;
  - secondly, it is intended to go beyond a palliative therapy, but a curative one, since the "specific tolerance" effect has been shown to last over time in in vivo models.
- Besides those advantages over the standard of care treatments, the Platform also has competitive advantages compared to other therapies working in the ASIT field:
  - Regime for human translation: reverse vaccination (3-4 doses 1 month) plus chronic boosts every 6 months/1 year.
  - Robust and cross the board MoA involving DCs- Tregs and also B cells.
  - Multiple Antigen strategy potential: our liposomes can encapsulate more than one antigen.
  - Versatility: Ahead technology does not depend on the HLA genotype of the patient.
  - Synthesis/manufacturing scale-up: liposomes manufacturing technology is a mature and proven technology.
  - Product/Treatment cost: liposomes are cheap to produce comparted to coated metallic and complex nanoparticles that are very expensive.
  - Tech-platform potential: only changing the auto-Ag we can address different indications.

IPR

Ahead's technology is widely protected through patent family WO2015107140. All the developed products to address all the indications selected in Ahead's pipeline and future new programs are under the scope of this patent.

It has been granted in Europe, Japan, China, Australia, and Mexico and is under prosecution in the US, India and Brazil. FTO analysis for the leading assets (RA and MG) has been done, and no operational conflicts have been detected.

PARTNERING OPPORTUNITIES

Ahead's business strategy consists of creating value to assets to make them go forward in the regulatory path until reaching clinical trials in humans, at which time their market value is multiplied.

Ahead has been active in business development. We have attended BIO, RESI, and JPMorgan conferences since the company's creation. We have met with Novartis, Mitsubishi Tanabe, Pfyzer, Grifols, MERCK, Eli Lilly, J&J, Abbvie, SANOFI, TAKEDA, and others. The result is that we perform regular updates with most of them, and we have established an MTA with one to explore our technology potential.

Resources needed are 17,5M€ for the 2022-26 period to reach CI. Phase Ib\IIa completed for RA and take MG until IND (8M€ for the 2022-24 period / 9.5M€ for 2024-26).

PROFILE

CIC bioGUNE, member of the Basque Research and Technology Alliance (BRTA), is a key research center within the national and international scientific landscape and has emerged as a knowledge source in the area of health science. The cutting-edge scientific activity of CIC bioGUNE researchers explores the interface between Chemistry, Structural, Molecular and Cell Biology, with the aim of developing a more Precise Medicine for the future. Whitin it, the Liver Disease Lab focuses on developing and promoting a range of high-quality, life-enhancing medicines to combat liver disease at every stage.

SPEAKER

Malu Martinez-Chantar is head of Liver Disease Lab at CIC bioGUNE. Professor Martinez-Chantar has an extensive experience in the study of liver biology and disease with a high-level track of productivity. She has been continuously supported by competitive public and private funding, both national and international. She coordinates the Translational Area of the National Institute for the Study of Liver & Gastrointestinal Diseases and shows extensive participation in different networks (CiberEHD, Women in Hepatology: International Consortium, Hepamet Registry, MetaboCancer Excellence Network and diverse EU COST actions). Her contracts with pharmas, as AGIOS, Mitotherapeutix, Takeda or Silence Therapeutics, led to 5 patent applications and 2 licensed products. Her collaboration with OWL Metabolomics led to the development of OWLiver® Care and OWLiver®, non-invasive assays for NASH diagnosis.

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PRODUCT

siRNA-based therapeutics to treat liver diseases

MECHANISM OF ACTION

Increased serum magnesium levels have been determined in pathophysiological conditions such as NAFLD, fibrosis, cirrhosis, cholangiocarcinoma, acetaminophen overdose and alcoholic liver disease. Besides, increased CNNM4 expression and protein levels were observed in the aforementioned pathologies, both in patients and in preclinical models resembling human pathologies.

The molecule target (a magnesium transporter CNNM4) modulates magnesium homeostasis in the liver. This transporter was identified by our laboratory and its altered hepatic expression has been associated with liver pathologies. Following the onset of liver injury, silencing of CNNM4 by GalNac, reverses liver pathologies by alleviating magnesium alterations in hepatocytes.

Our molecule is a therapeutic small interfering RNAs targeting the gene (CNNM4) which is bound to a N-acetylgalactosamine (GalNAc) molecule and stabilized with specific building blocks. The GalNAc molecule is specifically recognized by the Asialoglycoprotein receptors, which are expressed specifically in the hepatocyte membrane, conferring a high specificity and effectiveness in the release of the cargo. The molecule enters the cell through endocytosis, therapeutic RNAs are liberated, and targeted gene is silenced.

TARGET INDICATIONS

Our molecule is effective in treating fibrosis, and the rare liver cancer cholangiocarcinoma. Preclinical studies are currently ongoing in alcohol hepatitis and acute liver failure for acetaminophen overdose.

CURRENT STATUS

- We have performed in vitro and in vivo studies to show the efficacy of GalNac-CNNM4 molecules, and we have observed:
  - Fatty liver: significant reduction in lipid content, inflammatory response, and fibrosis in the liver parenchyma Simon et al Journal of Hepatology 2021.
  - Alcoholic liver disease: significantly reduced liver injury, lipid accumulation and inflammation manuscript under preparation.
  - Drug induced liver injury: significantly reduced necrotic liver injury and enhanced regenerative response manuscript under revision Nature Communication.
  - Cholangiocarcinoma: increased survival rate and significant tumour regression.
- Additionally, we are raising funds for the regulatory road map, GLP and GMP production, toxicity and patents maintenance.

INNOVATIVE ASPECTS

- The main differences from other current drugs are cell specificity (direct targeting of the hepatocyte); stability (in the bloodstream the stability of the molecule was approximately one-month), administration (subcutaneous); lack of toxicity (approved by the FDA and EMA); and increased efficacy.
- In addition, the effectiveness of the molecule has been tested in various stages of the disease, from the initial to more aggressive conditions caused by various etiologies.
- Since it is a chemically synthesized product, the cost is lower compared to biological products.

IPR

We have two patents: 1) Methods for diagnosis and treating acute on chronic liver, kidney or lung disease (WO2020109316A1) with priority filing Nov 2018. Patent is entered into national phases in 15 countries; 2) Nucleic acids for inhibiting expression of CNNM4 in cell (WO2021239825A1) with priority filing May 2020 and National phase entry by Nov 2022.

PARTNERING OPPORTUNITIES

Co-development agreements with Pharma can bring expertise in preclinical regulatory development, and Clinical Trial expertise, as well as pricing and market access knowledge.

PROFILE

Institut d'Investigació Biomèdica de Bellvitge

The **Bellvitge Biomedical Research Institute** (IDIBELL) is a biomedical research center created in 2004. It is participated by the Bellvitge University Hospital and the Viladecans Hospital of the Catalan Institute of Health, the Catalan Institute of Oncology, the University of Barcelona and the City Council of L'Hospitalet de Llobregat. IDIBELL research is focused on cancer, neuroscience, translational medicine and regenerative medicine. Within it, the "Immune-inflammatory Processes and Gene Therapy research group" carries out translational research with a primary focus on the molecular basis of immune-inflammatory processes. Its aim is to promote relevant, high-quality research into inflammation and to provide an optimal environment for training young researchers.

SPEAKER

Josep M. Aran (Ph.D.) is a Research Professor (R4-IDIBELL) and head of the "Immune-inflammatory Processes and Gene Therapeutics" group (IDIBELL). Dr. Aran holds more than 20 years expertise in the immune-inflammatory processes field, focused on the characterization of novel biomolecules, and in the development of diagnostic and therapeutic strategies for acute and chronic inflammatory conditions. He has been awarded with 26 translational research Projects as PI, published 66 research papers in leading biomedical journals (31 as corresponding author), authored several book chapters and journal reviews, holds 9 international patents, and has supervised 10 PhD students. Dr. Aran was co-founder and partner of "Zyrnat Biotherapeutics, S.L." (spin-off; biopharmaceuticals R&D). He has also licensed several of his patents to biotech companies: "Histocell", "Spherium Biomed", "Paperdrop Dx".

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PRODUCT

PRP6-HO7: a first-in-class biologic immunomodulator against autoimmune diseases

MECHANISM OF ACTION

PRP6-HO7, is a human recombinant protein derived from the classical complement inhibitor isoform C4BP(β-) (PRP-HO7), stable in the circulation and with sustained action to treat autoimmune diseases (AD). The primary indication will be the induction and maintenance of clinical remission of adult patients with moderate to severe IBD. Some of them have had an inadequate response, lost response, or have become intolerant to conventional therapies.

The PRP6-HO7 molecule has a novel mechanism of action (MoA) as immunomodulator able to "metabolically reprogram" key cells orchestrating the immune response toward operational tolerance. Due to its unique MoA, this biologic can be administered alone or in combination with other treatments in patients who do not respond to a single therapy. Furthermore PRP6-HO7, being smaller than an antibody and non-glycosylated, will reduce drug development costs compared to existing therapies.

TARGET INDICATIONS

First-in-class biologic (recombinant protein) for the treatment of a wide range of autoimmune diseases (systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis, dermatitis, …) and other immune-mediated inflammatory conditions.

CURRENT STATUS

- PRP6-HO7 has successfully been produced in eukaryotic and bacterial cells, purified, and tested in vitro and in vivo, in an acute IBD model. Also, a predictive end-point bioassay has been developed to assess PRP6-HO7 efficacy/response in blood samples from AD patients.
- Valorization actions developed:
  - Purification (human serum), production (HEK293 cells) and characterization of the immunomodulatory activity of PRP-HO7 in human monocyte-derived dendritic cells (Mo-DCs) and monocyte-derived macrophages.
  - Preclinical assays assessing safety and efficacy of PRP-HO7 in 3 mouse models of AD (lupus nephritis, acute IBD and rheumatoid arthritis).
  - Design, synthesis and pilot production of PRP6-HO7 in HEK293 and bacterial cell systems.
  - Characterization of the immunomodulatory activity of PRP6-HO7 in human Mo-DCs and Mo-macrophages from lupus nephritis patients.
  - Development of a predictive end-point bioassay (blood test) to assess PRP6-HO7 efficacy/response from IBD patients in advance to prospective PRP6-HO7 clinical trials.
  - MoA of PRP6-HO7: identification and characterization of the cell surface receptor and signaling pathways responsible for the immunomodulatory activity of PRP6-HO7.

INNOVATIVE ASPECTS

- This analogue is very attractive. It binds to human monocytes differentiating to dendritic cells and macrophages and can modulate its pro-inflammatory maturation/polarization with high efficiency.
- Current therapies have low safety profiles, low patient adherence to treatment due to toxicity, and can cause immunosuppression, leading to severe treatment-emergent adverse events (TEAE), which results in discontinuation of treatment in a significant number of patients.
- Key opinion leaders emphasized that drugs with higher efficacy and better safety need to be discovered. Antibody-based biologics (infliximab, adalimumab, ustekinumab ...) have been introduced during the last decades. However, primary nonresponse is observed in 20-30% of patients, and another 30-50% of patients become refractory due to secondary loss of response.
- Our fist-in-class metabolic immunomodulator, PRP6-HO7, has proved highly efficacious, showing superior anti-inflammatory and tolerogenic activities than the standard of care (3 times higher efficacy compared to anti-TNF biologics, and 10 times more specific that the broad-spectrum immunosuppressor cyclophosphamide), and null toxicity by periodic subcutaneous administration in our preclinical assays.
- By having a better safety profile, we expect the drug to improve patient adherence.

IPR

Two patents have already been granted related to methods and strategies for immunomodulation, and a third patent has been requested for our improved lead molecule PRP6-HO7: EP11382240 (15/07/11) "Compositions and methods for immunomodulation"; EP17382187 (06/04/17) "C4BP-based compounds for treating immunological diseases"; EP19382910 (17/10/19). "Compounds for immunomodulation" PCT/EP2020/079374 (Submitted: 19-10-2020). The first two patents are already in national phases. Ownership of the IP: 100% IDIBELL.

PARTNERING OPPORTUNITIES

Our primary interest is a co-development partnership and/or licensing of our asset, but any other form of collaboration agreement will be welcome.