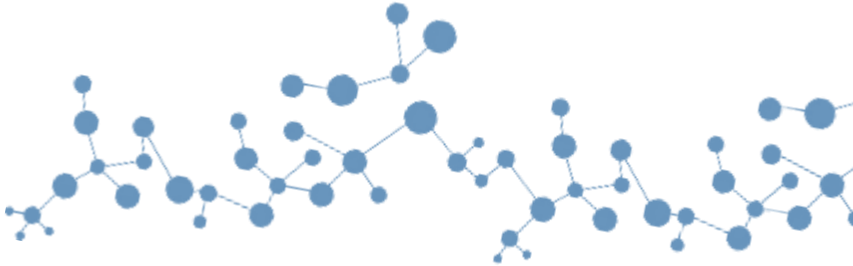
MEDESIS PHARMA
A clinical-stage drug delivery platform

Investor Presentation
March 2022

Disclaimer



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Medesis Pharma Presentation

medesis

Management

Management Board

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CEO, Chairman of the Board

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Director of Medical Affairs and Clinical Developments

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Member of the Management Board, Director of Strategic Partnerships

Tessa Olivato
Administrative and Financial Director

Supervisory Board

Olivier Connes
President of Supervisory Board

Bernard Connes | Jean-Marie Cazalèdes | Jean-Philippe Causse | Cédric Navas | Emmanuel Hebert

A committee of international experts

NEUROLOGIE

Pr. Jacques TOUCHON

Dean of the Faculty of Medicine from 2000 to 2010, head of neurology at Montpellier University Hospital, supervising the entire neurology department.
Alzheimer's Disease Clinical Trials Co-Chair
Co-editor of the Journal “Prevention of Alzheimer’s disease”

Pr. Serge GAUTHIER, C.M., MD, FRCPC

Currently Professor in the Departments of Neurology and Neurosurgery, Psychiatry and Medicine at McGill University, Director of the Alzheimer's Disease and Related Disorders Research Unit at the McGill University Research Center for Studies in Aging, Douglas Mental Health University Institute.

Pr. Guy ROULEAU, M.D.,Ph.D.,FRCPC

Director of the CHU Sainte-Justine Research Center and founder and director of the Center of Excellence in Neuroscience; he held the Canada Research Chair in Genetics of the Nervous System and the Jeanne-et-Jean-Louis-Lévesque Chair in Genetics of Brain Diseases. Medical degree (with great distinction) from the University of Ottawa and Doctor of Genetics from Harvard University. Officer of the National Order of Quebec and Fellow of the Royal Society of Canada (2016).

Pr. A. Claudio CUELLO, M.D., D.Sc., FRSC, OC

Former Chair of the McGill Department of Pharmacology and Therapeutics and currently Chair of the Charles E. Frosst Merck. He leads a research team working on the multidisciplinary aspects of brain repair, brain aging and the cellular and molecular neuropathology of Alzheimer's disease.

ONCOLOGIE

Pr. Gerald BATIST

Director of the Segal Cancer Center Director, Dept. of Oncology, Sir Mortimer B. Davis-Jewish General Hospital
Scientific Director of the Montreal Center for Experimental Therapeutics in Cancer, Director of the McGill University Center for Translational Research in Cancer
Chair of the Oncology Department, Professor, Department of Medicine and Oncology, McGill University.

Pr. Sylvie MADER

Full Member of the McGill Center for Translational Research in Cancer, Principal Investigator Molecular Targeting in Breast Cancer research unit, IRIC Professor, Department of Biochemistry, Faculty of Medicine, Université de Montréal Adjunct Professor, Department of Medicine, Experimental Medicine Program, McGill University Holder and Chair of the CIBC research chair on the causes of breast cancer.

Overview of Medesis Pharma

About

To further research of therapies for serious diseases for which there is no effective treatment, Medesis Pharma designs drug candidates based on its proprietary Aonys® technology. Aonys® enables administration of active ingredients nano-droplets by buccal route, allowing their delivery in all cells.

Neurodegenerative diseases: Alzheimer's Disease, Huntington's Disease
Virology: COVID-19, Influenza
Oncology : breast cancer, colorectal cancer, glioblastoma…
Nuclear decorporation and radiation protection

18 years of research
11 patents, 15 scientific publications
Partnerships with public and private laboratories

Bourse

€30m raised in pre-IPO, exclusively from private investors
€7.35m raised in February 2021 following the success of the IPO on EURONEXT Growth Paris® (€47.6m requested)

Label: MEDESIS PHARMA
Listing market: Euronext Growth Paris
ISIN Code: FR0010844464
Mnemo: ALMDP

Drug delivery pain points

Traditional routes of administration

Oral route is convenient but limited : absorption through the intestinal mucosa, first-pass metabolism the liver (drugs are partially degraded).

Injectable route (intravenous, intramuscular, subcutaneous): direct penetration of the drug and rapid action but impacting patients' quality of life.

Two major issues:

1. Cell penetration

General constraint regardless of the routes of administration: difficulty for pharmaceutical active ingredient to penetrates through cell membranes.

Very low intracellular penetration requires high therapeutic doses often responsible for drug toxicity. Most existing drugs target extracellular receptors.

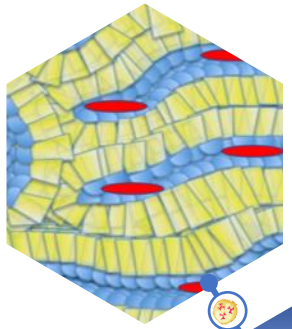
2. Crossing the Blood-Brain Barrier (BBB)

Almost all therapeutic molecules do not cross the BBB: need for intrathecal administration when targeting the central nervous system.

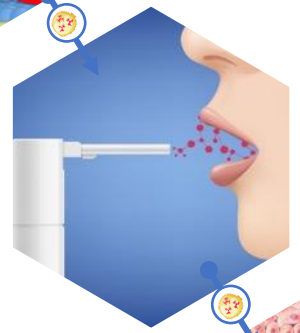
Aonys®, a drug delivery platform developed by Medesis Pharma, provides a solution to these constraints

Aonys® technology

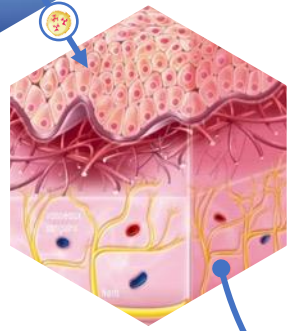
1 Definition and manufacturing of micro-emulsion

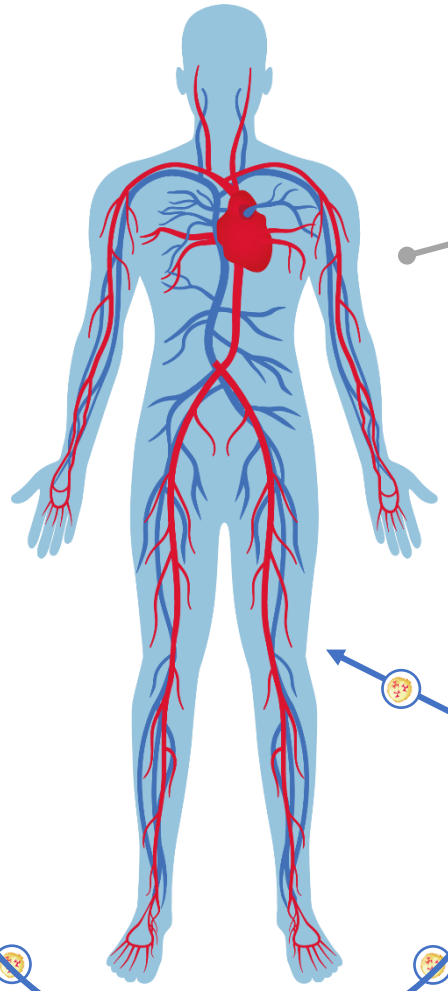


2 Simple delivery in the mouth

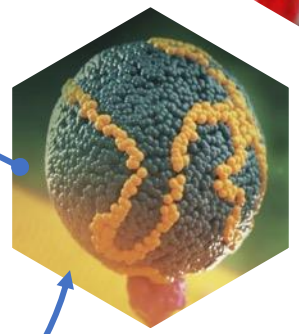


3 Absorption through buccal mucosa

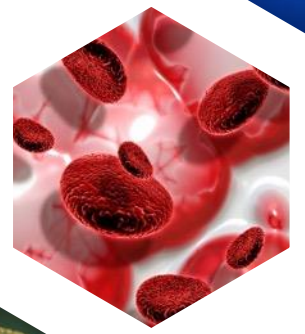




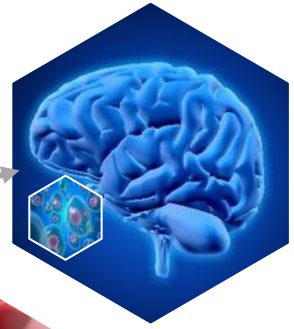
4 Structuration in HDL lipoproteins



5 Protected and invisible transport in lymphatic and vascular systems

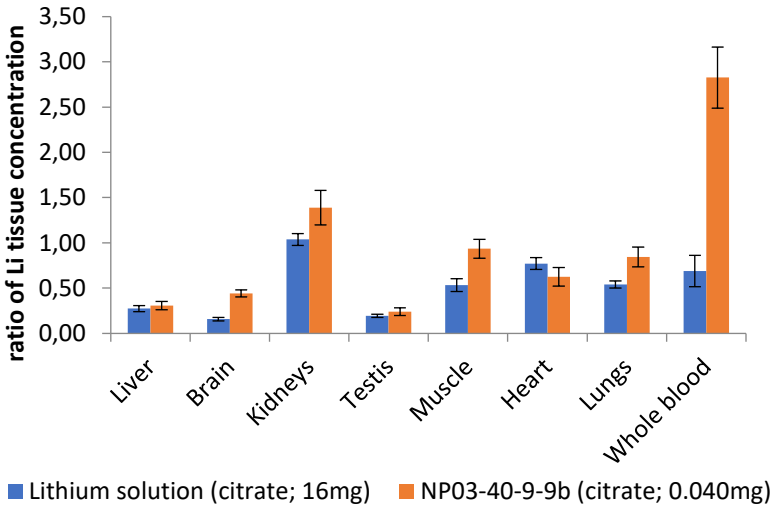


6 Internalization in all cells; with passage of Blood-Brain-Barrier



… from mouth to cells

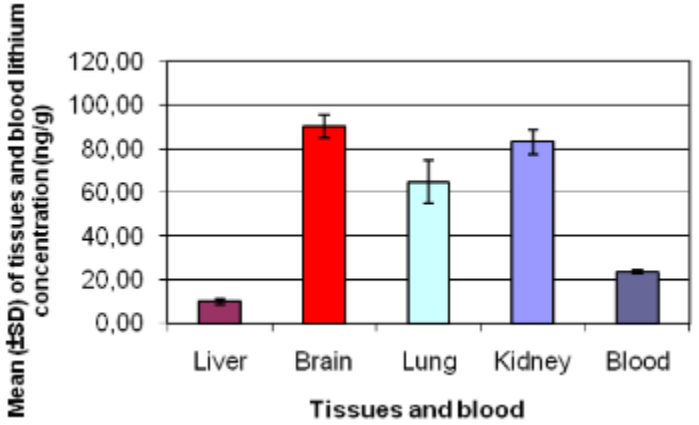
Aonys vs traditional solution



400 times less lithium in NP03

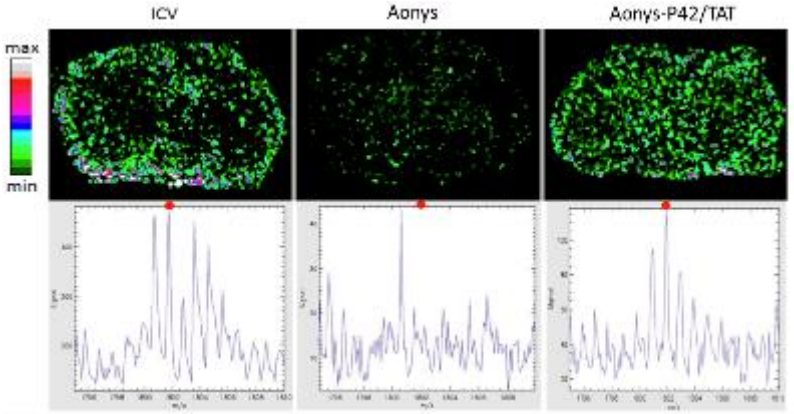
Lithium distribution after a 5-day repeated administration in mice.

Biodistribution in the organs



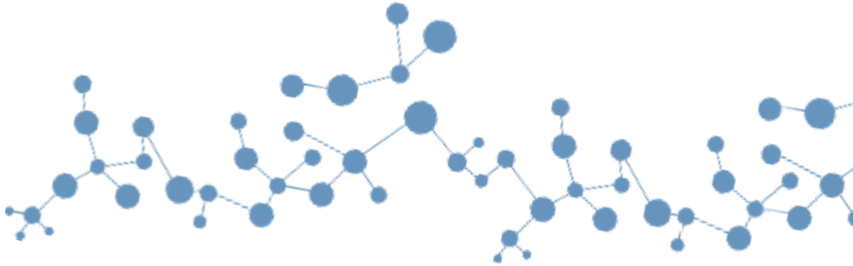
Lithium distribution after a 5-day repeated administration in mice.

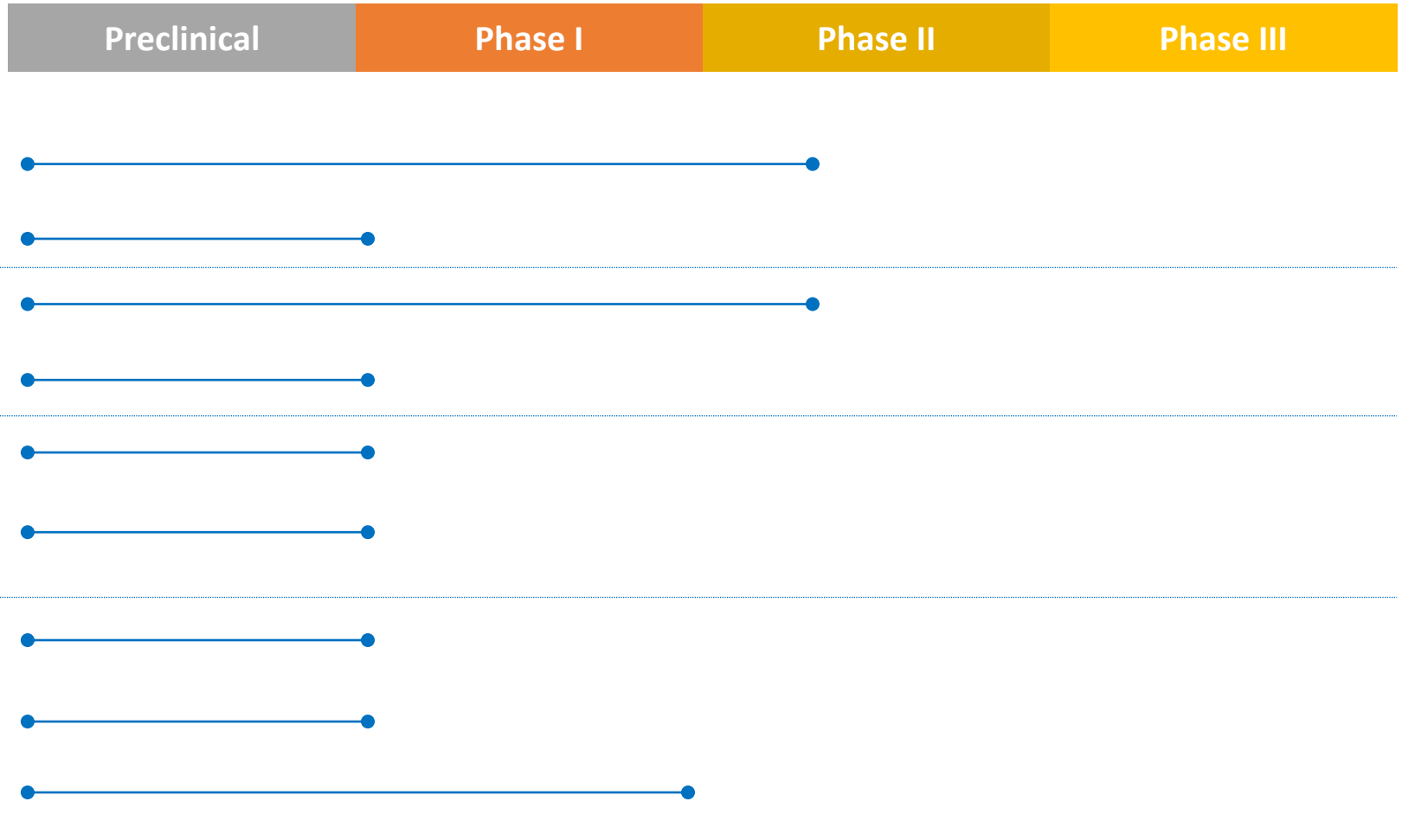
Penetration into the brain



Peptide distribution per IMS and Tissue View processing from wild-type mice injected by ICV, or treated with empty Aonys, or with P42T Aonys microemulsion

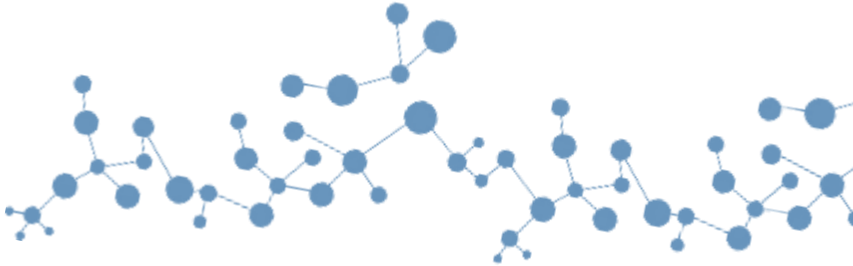
Pipeline




Preclinical
Phase I
Phase II
Phase III
Programs under development
NEURODEGENERATIVE DISEASES
Alzheimer NanoLithium
Huntington NanosiRNA
VIROLOGY
COVID NanoManganese
COVID et Influenza NanosiRNA
ONCOLOGY
TRANSGENE NanosiRNA
Radiotherapy Glioblastoma NanoManganese
NUCLEAR DECORPORATION
NU01 Plutonium decorporation
NU02 Cesium decorporation
NanoMn Radioprotection

2 Current clinical projects

NanoLithium®
ALZHEIMER'S DISEASE



Microemulsion Aonys® of microdosed lithium with buccal administration

- Pharmacological activity with 100 times less lithium in animals than for currently used lithium solution (the historic drug)
- No toxicity
- Acting at cellular level, after passage of the BBB, on pathological mechanisms involved in the disease

Stage of development

Phase 2 clinical study: in 6 university hospitals in France (Q2 2022)

3 months of treatment to observe effect on mental disorders, followed by 9 months open label treatment to look for a disease-modifying effect (change in the evolution of the disease on clinical outcomes, biomarkers, imaging…)

Therapeutic dose 32 times lower than the usual dose of lithium

Addressable market

+900,000 people affected in France (225,000 new cases / year)

30 million patients worldwide in 2030, 50 million in 2050

Strategy

Development in phase 2, indication: behavioral and psychotic manifestation associated with Alzheimer's disease

License transfer at the end of Phase 2

** Sources : France : Fondation Recherche Alzheimer*
Monde : Journal of Psychiatry « Market analysis alzheimer's disease 2020 », May 2020

NanoLithium®
Other potential clinical applications

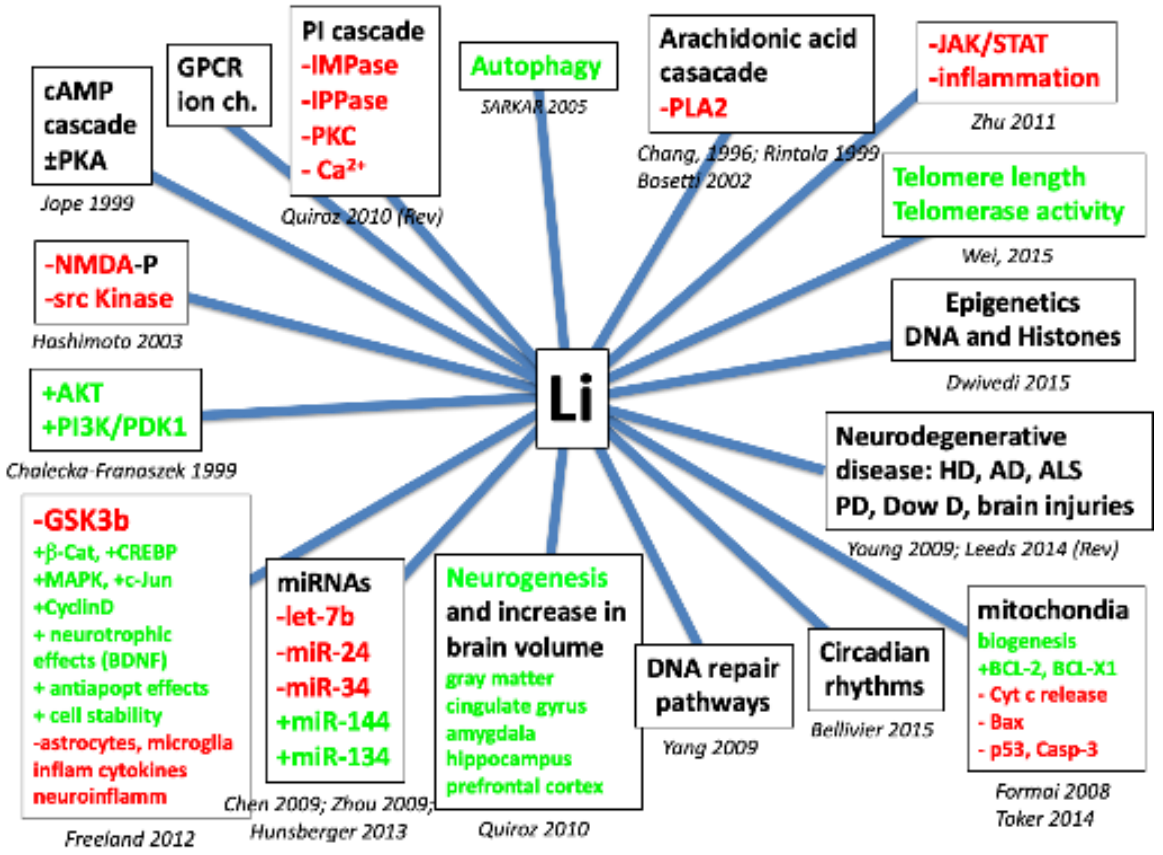
Possibility to clinically test Nanolithium in other pathologies deprived of effective treatment:

- >Huntington's disease
- >Amyotrophic Lateral Sclerosis
- >Cognitive disorders in Trisomy 21
- >Traumatic neuropathies

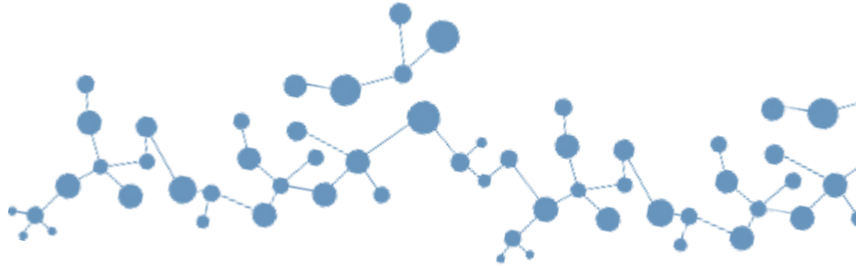
Stimulation of neurogenesis and important role in neuroprotection

More than 200 publications support potential therapeutic benefice in most neurodegenerative diseases

Concluding results of preclinical studies on animal models
conducted by Medesis Pharma on several neurodegenerative diseases without effective treatment



NanoManganese®
Complication of COVID-19 infection



Microemulsion Aonys® of microdosed Manganese with buccal administration

- "MnSOD like" activity demonstrated in preclinical studies
- Regulation of the inflammatory cytokine storm responsible of COVID-19 complications (i.e. Acute Respiratory Distress Syndrome)
- Viruses can inhibit MnSOD* activity, becoming more aggressive
- MnSOD acts as the main ROS (reactive oxygen species) scavenging enzyme in the cell => preserving cellular and organs of oxidative stress, ionizing radiation and inflammatory cytokines.

Stage of development

Phase 2 in progress in Brazil in 8 hospitals: 120 patients being included (90 NanoManganese 30 placebo). Treatment initiated during hospitalization. Results expected summer 2022

Addressable market

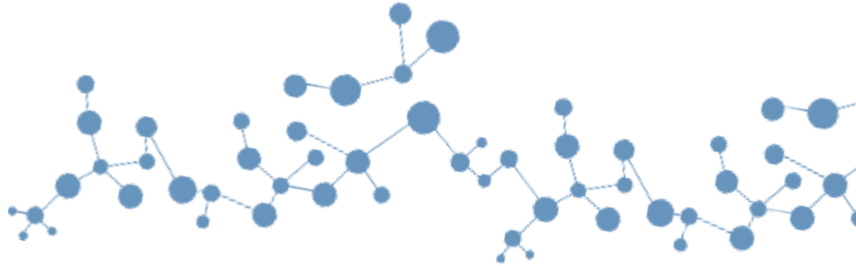
+100 million people infected (world)

Strategy

With positive results, a phase 3 will be initiated for the same indication or for the treatment of severe forms of other viral diseases, such as influenza

** Source : W.H.O. Coronavirus dashboard – GEODES Santé publique France, Oct. 2020*

NanoManganèse®
Other potential clinical applications



Optimization of cancer radiotherapy

Efficacy of NanoManganese for the protection of healthy peritumoral tissues during radiotherapy of a tumor
A first study showed the maintenance of the effectiveness of radiotherapy on a transplanted glioblastoma

Graft versus Host Disease (GvHD)

Important cause of morbidity and mortality after allogenic hematopoietic stem cell transplantation
GvHD pathophysiology involves cytokine storm

Cytokine Release Syndrome caused by immunotherapies (CAR-T)

CAR-T cells eliminate tumor cells expressing targeted antigen, but simultaneously they proliferate and release a variety of inflammatory factors triggering a systemic inflammatory response that can be life threatening.

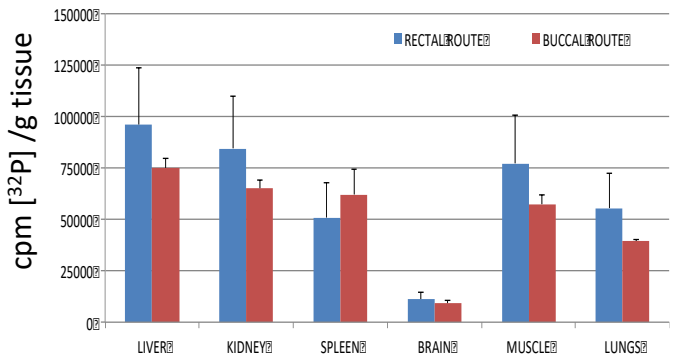
Radiation protection and radiation mitigation during an accident on a nuclear reactor

3 A drug delivery platform for siRNAs

AONYS® siRNA Delivery Platform

Small interfering RNAs (siRNAs) are small double-stranded RNAs.
They can inhibit the expression of a gene by directing the cutting (or cleavage) of RNAs which are complementary to them or by inhibiting the translation of a specific genetic sequence.
They are degraded in living organisms as soon as they are administered by RNAse. In IV or IM injection, they trigger an immune reaction (RNA vaccines)
Aonys® technology enables the delivery of unmodified native siRNAs directly into the cytoplasm of all cells of the body through HDL lipoprotein receptors, with passage of the BBB after a non-invasive buccal administration.
Several animal studies have demonstrated efficient inhibition of targeted gene with siRNAs formulated in Aonys

Biodistribution of Aonys®-32P-siRNA (1mg/kg) - 24h post administration

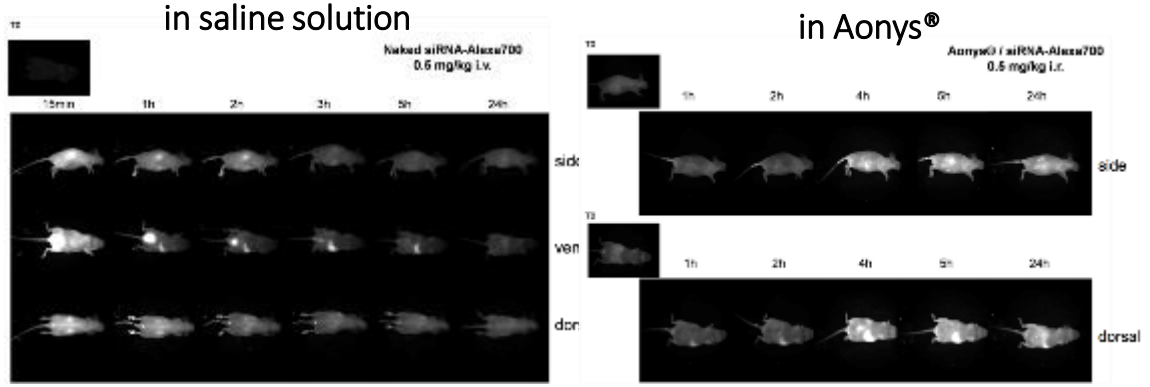


Aonys®-siRNA is delivered in all organs

Biodistribution of Aonys®- FluosiRNA (1mg/kg) - 24h post administration

Fluorescence of labelled siRNA in saline solution

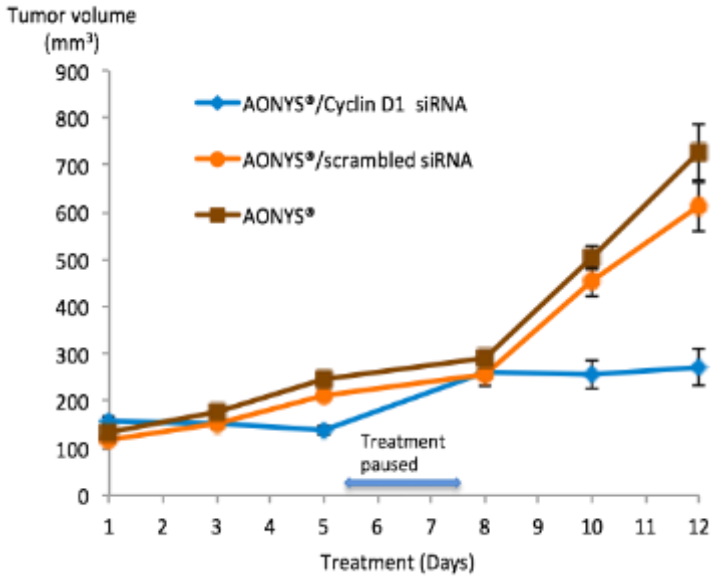
Fluorescence of labelled siRNA in Aonys®



Simple intravenous administration of unmodified siRNA results in rapid renal clearance and limited tissue distribution. Rectal administration of the same unmodified ARNi formulated in Aonys® shows complete absorption together with extensive and prolonged tissue distribution.

AONYS® siRNA Delivery Platform :
Future developments

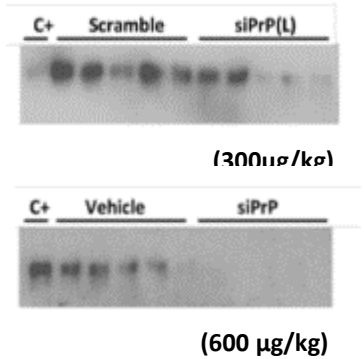
Oncology



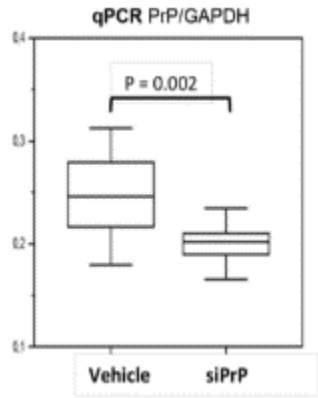
Effect of siRNA against CCND1 gene after a 12-Day administration in wild-type mice

Neurodegenerative Diseases

PrP levels evaluated by western-blot



PrP mRNA levels (ELISA)



Effect of siRNA against PrP(C) gene in brain tissues after a 12-Day administration in wild-type mice

Virology

Aonys® microemulsion of unmodified native siRNAs preventing viral replication by targeting a major protein of the virus, with buccal administration .

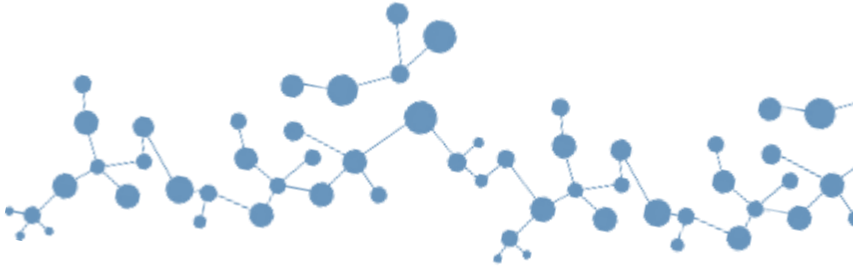
Ongoing preclinical study on COVID-19

Scientific publications

Lehmann S, Relano-Gines A, Resina S, Brillaud E, Casanova D, Vincent C, Hamela C, Poupeau S, Laffont M, Gabelle A, Delaby C, Belondrade M, Arnaud JD, Alvarez MT, Maurel JC, Maurel P, Crozet C. Systemic delivery of siRNA down regulate brain prion protein and ameliorates neuropathology in prion disorder; PLoS One. 2014 Feb 14;9(2):e88797

J. Champagne, L.K. Linares, B. Maurel, A. Zampieri, M. Moreno, I. Fuentes, E. Dubois, D. Severac, A. Decorsiere, F. Bienvenu, TAG-RNAi Overcomes Off-Target Effects in Cancer Models; Oncogene; 2020 Jan;39(4):935-945.; doi: 10.1038/s41388-019-1020-2. Epub 2019 Sep 26

NanosiRNA HD
Huntington’s disease treatment



An Aonys® microemulsion of unmodified native siRNAs for buccal administration specifically targeting a sequence of the mutated Huntingtin (HTT) gene.

Huntington’s Disease is a heterozygous disease: there is a mutated allele that is dominant and a wild-type one. The wild-type one is essential to normal cellular functions.

The HTT gene contains few SNPs (single nucleotide polymorphisms) with allele frequencies in the human population. It is thus possible to specifically target the mutant mRNAs with an allele-specific RNAi directed against the SNPs. Because the link between individual SNPs and mutated allele depends on each patient's genetic information, it will be necessary to sequence patient's HTT locus before choosing siRNAs to administered. 5-8 siRNA can target more 90% of Huntington’s Disease.

Stage of development

Favorable opinion from the European Medicines Agency (EMA) on May 27, 2021

Next steps envisaged

- CMC siRNA development and finished product: Q2 2022 to Q2 2023
- PK development and toxicology: Q3 2022 to Q3 2023
- Phase 2 clinical study: Q4 2023 to Q3 2024

4 Preclinical projects and collaborations

siRNA Delivery Platform
Preclinical projects and collaborations

NanosiRNA COVID

Aonys® microemulsion of unmodified native siRNAs preventing viral replication by targeting a major protein of the virus, with buccal administration .

Goals :
Specifically targeting the gene for the largest protein in SARS-Cov-2, not mutated in identified variants.
Preclinical study (contaminated animal model) in progress
Evidence the possibility to treat viral diseases through siRNA (Potential for developments in influenza, childhood pneumopathy, dengue fever, smallpox, etc.)

NanosiRNA oncology

Collaboration with TRANSGENE:
Ongoing collaborative program on siRNAs formulated in Aonys to inhibit expression of antiviral proteins that reduce the effectiveness of oncolytic viruses.

5 Nuclear accident drug programs

Collaborations with Commissariat à l'Energie Atomique (CEA) and institut de Recherche Biomédicale des Armées (IRBA)

medesis

Radionuclide decorporation treatment

Radionuclide decorporation treatment,
suitable for large populations contaminated during a civil or military nuclear accident

NU01 Plutonium decorporation & NU02 Cesium decorporation

MEDESIS PHARMA is developing two assets for protection of populations who have been contaminated during a nuclear accident (CEA collaboration):

- Decorporation of Plutonium
- Decorporation of Cesium

Objective :

Treating large populations contaminated after a nuclear accident

NP02 Radioprotection

MEDESIS PHARMA is developing a radiomitigation treatment administered during or within minutes/hours following overexposure to ionizing radiation

Objective:

Treatment of civilian and military personnel (dual technology) subjected to irradiation, whether industrial, medical, accidental or intentional, and whether external or internal (IRBA collaboration)

6 Markets addressed by Medesis

Key figures

NanoLithium®
ALZHEIMER'S DISEASE

Adressable market*: + 900,000 people affected in France (225,000 new cases/year).

30 million patients worldwide in 2019, 50 million in 2030.

Strategy: License transfer at the end of Phase II

** Sources : France : Fondation Recherche Alzheimer*
Monde : Journal of Psychiatry « Market analysis alzheimer's disease 2020 », May 2020

NanosiRNA® VIROLOGY
COVID-19 and Influenza (early treatment)

Adressable market*: +1 million new Covid-19 cases per day (world) including 50,000 in France

3 to 5 million serious cases of influenza per year in the world

Strategy: License transfer at the end of Phase II

** Source : W.H.O and Our Wolrd in Data*

NanoManganese®
COVID-19 serious clinical forms

Adressable market*: +1 million new cases per day (worldwide) including 50,000 in France

Strategy: License transfer at the end of Phase II

** Source : Our world in data, Fev. 2022*

NanosiRNA® HD
HUNTINGTON'S DISEASE

Orphan drug

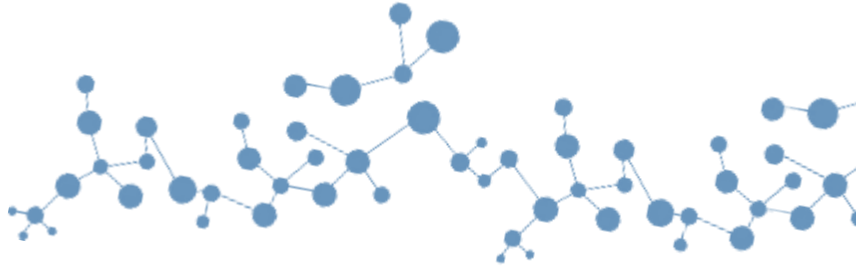
Adressable market*: approximately 5 cases per 100,000 individuals (worldwide) 18,000 people concerned in France (approximately 6,000 symptomatic and approximately 12,000 carriers of the mutated gene). 100,000 EU and USA patients

Strategy: Pharma partner upon preclinical positive outcomes incl. license option post clinical proof of concept

** Sources : Orphanet*

7 Appendices

Intellectual Property



11 patents in force on the technology and its functionalities

Code	patent title	Country, date and number
B191	Manganese based organometallic complexes, pharmaceutical compositions and dietetic products	Israël : 01/10/2012, n°170516
B316	Reverse micelles based on phytosterols and acylglycerols and therapeutic uses thereof	Canada : 07/01/2014, n°2584980C Israël : 30/03/2012, n°182747
B315	Reverse micelle composition for delivery of metal cations comprising a diglyceride and a phytosterol and method of preparation. Methods for preparing reverse micelles based on sterols and acylglycerols for the delivery of metal ions	Chine : 24/08/2011, n°101102751B Israël : 29/05/2011, n°182756
B1013	Reverse micelle system comprising nucleic acids and use thereof	Etats-Unis : 04/11/2014, n°8,877,237B2 ; 27/09/2016, n°9,452,136 B2 Europe (16 pays) : 09/11/2016 ; n°2549980B1 Japon : 07/12/2016, n°6038017B2
B1012	Reverse micelle system comprising metal ions and use thereof	Europe (18 pays) : 08/07/2015, n°2550020B1 Etats-Unis : 14/03/2017, n°9,592,218B2
B1777	Use of reverse-micellar system for delivering chelators of radionuclides and metals	Afrique du Sud : 20/12/2017, n°2016/06346 *Demandes : Canada, Chine, Corée du Sud, Etats-Unis, Eurasie, Europe, Israël.*
B2060	In situ preparation of cyano-bridged metal nanoparticles within a biocompatible reverse micellar system	*Demandes : Canada, Chine, Etats-Unis, Eurasie, Europe, Israël, Japon*
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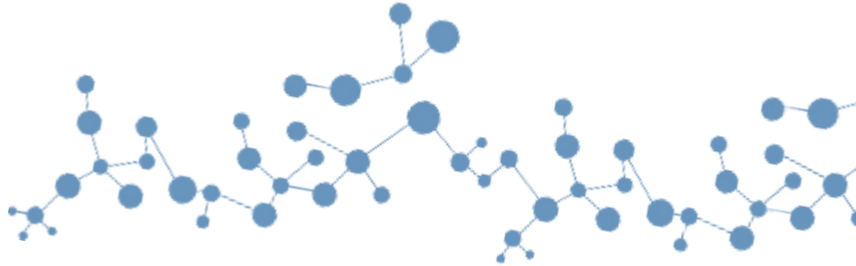

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