

Technology for the Treatment of Neurodegenerative Diseases Targeting Alzheimer's Disease

Presentation by Dr. Francis Marsais

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ABOUT ALZEX BIO MEDICAL & VFP THERAPIES

ALZEX BIOMEDICAL GROUP is a private company that has entered into an agreement with a French Biotech Company, VFP THERAPIES

ALZEX is a collaboration of researchers, scientists, and investors that have developed and patented precision therapeutics for the treatment of Alzheimer's Disease (AD) and other neurological diseases

ALZEX currently holds a multiple family of patents

Our North American headquarters is located in Vancouver B.C with our subsidiary VFP THERAPIES laboratories located in France (Normandy)



ALZHEIMER'S DISEASE: LOSS OF THE HUMAN MIND



- The gradual deterioration of a lifetime's worth of wisdom, experience and personal relationships
- 50 million people worldwide and six million Americans are living with AD, and the number is expected to rise sharply
- China: 9,5 million sufferers (more than twice) 1 million new ones /year
- China: Major healthcare problem Very few specialised care available
- 2050 Forecasting¹: 115 million patients worldwide and US\$ 2,000 billion (global cost)
 - ¹ World Health Organization December 2017 World Economic Forum – September 21, 2017



SEARCHING FOR THE CURE

Accumulation of toxic proteins causes the formation beta amyloid plaques or tau tangles Death of cholinergic neurons = cognitive deterioration & emergence of dementia symptoms

- * Neurotransmitter modulation for symptomatic therapies: commercial drugs (Aricept[®], Exelon[®]...)
- * Disease-modifying therapy targeting amyloid and tau = protection and removal of toxic materials The search for a drug to treat AD, the most common form of dementia, has been marked by many clinical trial failures (> 99,6%): one says that AD is a "Cemetery of Drug Candidates"
 - Ex.: Eli Lilly has just dropped a BACE inhibitor in combination with a monoclonal antibody (phase 3)
 - Whatever the most significant therapeutic discoveries in the future there will always remain a strong need for safer drugs to allow the symptomatic treatment of Alzheimer's disease

ALZEX challenge = Designing innovative safer drugs to substitute the current ones by limiting the current noxious side-effects





OUR BIOPRECURSOR

We have developed innovative drug candidates called Bioprecursors

Bioprecursor = Improved prodrug (drug de novo and not a simple delivery system)

VFP THERAPIES Innovative Concept of Bioprecursor

- Chemically masked form of a biological active molecule
- No recognition by the biological receptors
- Lipophilic small molecule crossing the Blood Brain Barrier (BBB)

Bioprecursor Activated inside the Brain: biological oxidative pathway

- Recognition by the biological receptors
- Induction of the targeted pharmacological effects
- Limitation of peripheral side-effects

Proof of Concept is achieved

- Successful design of new drugs for AD mimicking commercial ones
- Bioprecursor technology can be applied to other brain diseases





BRAIN TARGETING BIOPRECURSOR

Shivering (Central effect)

Biological trials on Mice and Rats are successful

- Bioprecursor (blue bars) reaches the brain
- Bioprecursor is activated into API: central effects are observed
- Improvment of the targeted enzyme inhibition: => 10 times
 lower isoactive dosis
- No longlasting peripheral side-effects

"Our Bioprecursor should be able to deliver symptomatic relief for a far longer period and at a far lower dosage Our Bioprecursor may present a new, safe way to mimic the current AD drugs, such as Aricept or Exelon"

Dr. Francis Marsais





Salivation (Peripheral effect)



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R & D RESULTS

- **1. DONE:** We have developed innovative drug candidates called BIOPRECURSORs
- 2. DONE: Proof of concept has been successful on animals by any administrative way (Irwing test)
- **3. DONE:** Selection of some lead molecules through supplementary trials:
 - ✓ Physicochemical optimisation: solubility, stability...
 - ✓ Biological screening in order to avoid undesirable biological effects: genotoxicity, enzymatic screening
 - ✓ The risk of failure has been anticipated by preparing backup molecules
- 4. UNDERWAY: Preclinical Assays: the selected leads molecules (possible drug candidates) are currently subjected to preclinical studies

The main goals of pre-clinical studies are to determine the safe dose for first-in-human studies and assess the product's safety profile

As they are mimicking commercially well known AD drugs (Aricept / Esai-Pfizer and Exelon / Novartis) with similar biological targets, we will take advantage of known animal models for the first phases and clinical development programs for the clinical phases

Our Goal = Push at least one drug candidate into Phase 1 (12 months) and complete Phase 1 (24 months)





WORLDWIDE PATENTS

PATENT 1

Patent **WO2006/102130** has been filed in 2006 by the INSA of Rouen (my academic establishment) and it has been totally repurchased in 2014 by VFP Therapies

It covers a large family of drug candidates which could be marketed in future to compete commercial drugs like Exelon[®]

The patent has been granted in the main worldwide countries and the annuities have been regularly paid (Australia, Canada, Europa, Israel, New-Zealand, Republic of South-Africa, Singapore and United States of America)

A second family of drug candidates issued from the parent patent has been developed to optimize the biological behavior This new family has been exemplified, 3 leads have been identified and a selection patent should be filed in 2019



PATENT 2

Patent **WO2014/114742** has been filed (PCT) by VFP Therapies 70% and its academic partners 30%

It covers a large family of drug candidates which could be marketed in future to compete commercial drugs like Aricept[®]

The PCT procedure has been launched in January 2015, the patent has been granted in United States of America, Canada and Europe



VFP THERAPIES: SCIENTIFIC R&D MANAGEMENT



Dr. Francis Marsais, Founder & CEO Ph.D. in Organic Chemistry

Former director of an important academic research group within the Institut de Recherche en Chimie Organique Fine (13 years)

Former director in charge of partnerships at the Institut National des Sciences Appliquées (5 years)

Author of over 130 international papers and holds 5 patents



Dr. Vincent Gembus, CSO Ph.D. in Organic Chemistry

Manager of various R&D project in medicinal chemistry on behalf of pharmaceutical partners Author of high level international papers Excellent experience of the pharmaceutical development & Key leader of the R&D team



FRENCH SCIENTIFIC, TECHNOLOGICAL & FINANCIAL PARTNERS











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SCIENTIFIC AND BUSINESS PROJECTS

- With the benefit of over ten years of research in France, the VFP Therapies approach brings an innovative response to minimizing the noxious side-effects of drugs as well as overcoming crossing the Blood-Brain-Barrier issue. The completed R & D studies have already demonstrated the technical proof of its concept in initial *in vitro* and *in vivo* models (mice & rats)
- The R&D target = achievement of preclinical assays and successful phase 1 trials
- Such a record, if positive, will allow to enter into discussions with pharmaceutical companies either to license our families of products or to negotiate a co-development program for their own Alzheimer drugs or other treatments for central nervous system diseases
- The current ALZEX short and mid-term expectations:
 - Fulfill an ongoing fundraising round (over \$ 10 million): contact ALZEX
 - Negotiate a Patent Operating Licence (upfront payment & milestones): contact VFP Therapies
 - Find a pharmaceutical group to build a sustainable partnership: contact VFP Therapies



CAPITAL STRUCTURE

Current Offering

First Round: \$2,000,000 @ \$0.25 with a full warrant @ \$0.30 (8 million shares)

Second Round: \$3,000,000 @ \$0.50 with a full warrant @ \$0.75 (6 million shares)

Pre IPO Financing (Feb 2019) - \$5,000,000 @ \$1.00 with a full warrant @ \$1.50 (5 million shares)

Issued & Outstanding: (pre IPO) - 19,000,000

Warrants: 19,000,000

Fully Diluted: 38,000,000



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