



ALZEX
BIOMEDICAL

Technology for the Treatment of Neurodegenerative Diseases

Targeting Alzheimer's Disease

针对阿尔茨海默症的
神经退行性疾病治疗技术

Presentation by Dr. Francis Marsais

报告人：Francis Marsais博士

FORWARD LOOKING STATEMENTS

前瞻性陈述

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ABOUT ALZEX BIO MEDICAL & VFP THERAPIES / ALZEX BIOMEDICAL 和VFP THERAPIES简介

ALZEX BIOMEDICAL GROUP is a private company that has entered into an agreement with a French Biotech Company, VFP THERAPIES / ALZEX BIOMEDICAL GROUP是一家私营公司，与法国生物科技公司VFP THERAPIES签订了协议

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在研究人员、科学家和投资者同心协力下，开发并获得了治疗阿尔茨海默症(AD)和其他神经疾病的精准疗法专利

ALZEX currently holds a multiple family of patents/ ALZEX目前握有多类专利

Our North American headquarters is located in Vancouver B.C with our subsidiary VFP THERAPIES laboratories located in France (Normandy) / 我们在北美的总部位于卑诗省温哥华，子公司VFP THERAPIES实验室位于法国（诺曼底）

ALZHEIMER'S DISEASE: LOSS OF THE HUMAN MIND

阿尔茨海默症：人类心智的丧失



- The gradual deterioration of a lifetime's worth of wisdom, experience and personal relationships / 患者毕生智慧、经历和人际关系都逐渐恶化
- 50 million people worldwide and six million Americans are living with AD, and the number is expected to rise sharply / 全球有5000万阿尔茨海默症患者，其中美国有600万，而且这个数字还将大幅上升
- China: 9,5 million sufferers (more than twice) – 1 million new ones /year / 中国：950万患者（两次以上）——每年新增100万
- China: Major healthcare problem – Very few specialised care available / 中国：主要医疗问题——很少有专门的医疗服务
- 2050 Forecasting¹: 115 million patients worldwide and US\$ 2,000 billion (global cost) / 2050年预测¹：全球阿尔茨海默症患者数量将达到1.15亿，医疗费用2千亿美元（全球成本）

¹ World Health Organization – December 2017 / 世界卫生组织——2017年12月

World Economic Forum – September 21, 2017 / 世界经济论坛——2017年9月21日

SEARCHING FOR THE CURE

寻求治疗方法

Accumulation of toxic proteins causes the formation beta amyloid plaques or tau tangles / 毒性蛋白的积累导致淀粉样蛋白斑块或Tau蛋白缠结的形成

Death of cholinergic neurons = cognitive deterioration & emergence of dementia symptoms / 胆碱能神经元死亡=认知能力下降和痴呆症状的出现

- * Neurotransmitter modulation for symptomatic therapies: commercial drugs (Aricept®, Exelon® ...) / 症状治疗神经递质调制: 商业药物 (Aricept®, Exelon®等)
- * Disease-modifying therapy targeting amyloid and tau = protection and removal of toxic materials / 针对淀粉样蛋白和tau的疾病修饰疗法=保护和清除有毒物质

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” / 寻求治疗最常见的痴呆症——阿尔茨海默症的药物在临床试验阶段基本上都失败了 (超过99.6%) : 有人说阿尔茨海默症是“候选药物的墓地”

Ex.: Eli Lilly has just dropped a BACE inhibitor in combination with a monoclonal antibody (phase 3) / 例如: 礼来刚刚宣布放弃BACE抑制剂与单克隆抗体联合使用(第3期)的研发

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 / 无论未来最重要的治疗发现是什么, 对于更安全的治疗阿尔茨海默症症状的药物需求将一直强劲

ALZEX challenge = Designing innovative safer drugs to substitute the current ones by limiting the current noxious side-effects / ALZEX的挑战=设计创新和更安全的药物, 通过限制当前有害的副作用来替代现有的药物



OUR BIOPRECURSOR

我们的生物前体

We have developed innovative drug candidates called Bioprecursors / 我们已经开发了一种创新的候选药物，叫做生物前体

Bioprecursor = Improved prodrug (drug de novo and not a simple delivery system) / 生物前体=改良后的前体药物（全新的药物，而非一个简单的传递系统）

VFP THERAPIES Innovative Concept of Bioprecursor / VFP THERAPIES对生物前体的创新概念

- ❖ Chemically masked form of a biological active molecule/ 生物活性分子的化学掩蔽形式
- ❖ No recognition by the biological receptors / 不被生物受体识别
- ❖ Lipophilic small molecule crossing the Blood Brain Barrier (BBB) / 亲脂小分子穿越血脑屏障(BBB)

Bioprecursor Activated inside the Brain: biological oxidative pathway / 生物前体在脑内被激活：生物氧化途径

- ❖ Recognition by the biological receptors / 被生物受体识别
- ❖ Induction of the targeted pharmacological effects / 诱导靶向药理作用
- ❖ Limitation of peripheral side-effects / 限制外周副作用

Proof of Concept is achieved / 已经实现了对这一概念的验证

- ❖ Successful design of new drugs for AD mimicking commercial ones/ 模仿商业药物成功设计阿尔茨海默症新药
- ❖ Bioprecursor technology can be applied to other brain diseases / 生物前体技术可以应用于其他大脑疾病



BRAIN TARGETING BIOPRECURSOR

针对患者大脑的生物前体

Biological trials on Mice and Rats are successful / 在大鼠和小鼠身上的生物学试验已经成功

- Bioprecursor (**blue bars**) reaches the brain / 生物前体 (下图蓝色条) 到达大脑
- Bioprecursor is activated into API: central effects are observed / 生物前体被激活进入API: 可观察到中枢作用
- Improvement of the targeted enzyme inhibition: => 10 times
lower isoactive dosis / 靶向酶抑制作用改善: =>低等活度剂量的10倍
- No longlasting peripheral side-effects / 无持久的外周副作用

“Our Bioprecursor should be able to deliver symptomatic relief for a far longer period and at a far lower dosage

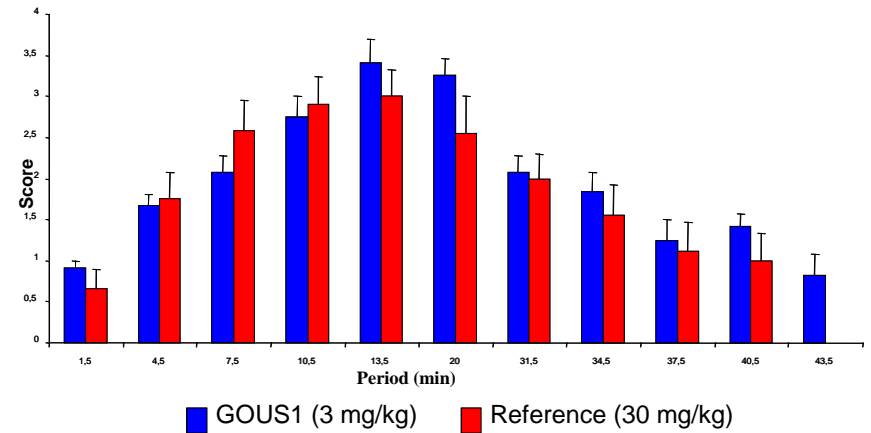
Our Bioprecursor may present a new, safe way to mimic the current AD drugs, such as Aricept or Exelon”

*“我们的生物前体药物应该能够在更长的时间内以更低的剂量缓解症状
我们的生物前体药物可能提供一种新的、安全的方法, 来模拟当前的阿尔茨海默症药物, 如Aricept或Exelon”*

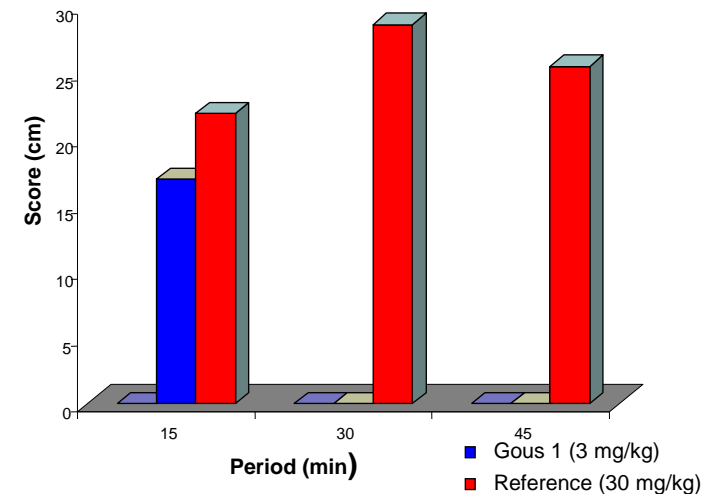
Dr. Francis Marsais / Francis Marsais博士



Shivering (Central effect)



Salivation (Peripheral effect)



R & D RESULTS

研发成果



- DONE:** We have developed innovative drug candidates called BIOPRECURSORS
已完成: 我们已经开发了一种创新的候选药物, 称为生物前体
- DONE:** Proof of concept has been successful on animals by any administrative way (Irwing test)
已完成: 已经成功在动物身上进行了试验, 验证了这一理论 (Irwing试验)
- DONE:** Selection of some lead molecules through supplementary trials: / **已完成:** 通过补充实验选出了一些先导分子
 - ✓ Physicochemical optimisation: solubility, stability... / 理化优化: 溶解性、稳定性等
 - ✓ Biological screening in order to avoid undesirable biological effects: genotoxicity, enzymatic screening/ 为避免不良的生物效应进行的生物筛选:基因毒性、酶筛选
 - ✓ The risk of failure has been anticipated by preparing backup molecules / 准备备用分子, 提前预见失败风险
- UNDERWAY:** Preclinical Assays: the selected leads molecules (possible drug candidates) are currently subjected to preclinical studies / **正在进行中:** 临床前试验:选定的先导分子(可能的候选药物)目前正在进行临床前研究
- 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 / 临床前研究的主要目标是确定首次人体试验的安全剂量并评估产品的安全性
- 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 / 当他们还在模仿商业上拥有相似生物靶点的知名阿尔茨海默症药物 (Esai-辉瑞的Aricept和诺华的Exelon) 时, 我们将利用已知的动物模型进行一期开发和临床阶段的临床开发活动。

Our Goal = Push at least one drug candidate into Phase 1 (12 months) and complete Phase 1 (24 months)
/ 我们的目标=将至少一种候选药物推入一期(12个月)并完成一期(24个月)

WORLDWIDE PATENTS

全球专利

PATENT 1 / 专利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 / 专利号**WO2006/102130**，由鲁昂的法国国家应用科学院在2006年提交，VFP Therapies在2014年完全回购

It covers a large family of drug candidates which could be marketed in future to compete commercial drugs like Exelon® / 该专利包含一大类的候选药物，这些药物未来可能问世并与Exelon®这样的商业药物展开竞争

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) / 该专利已被世界主要国家授予，年金已定期支付(澳大利亚、加拿大、欧罗巴、以色列、新西兰、南非共和国、新加坡和美国)

A second family of drug candidates issued from the parent patent has been developed to optimize the biological behavior / 由母专利产生的第二类候选药物正在研发，目的是优化生物行为

This new family has been exemplified, 3 leads have been identified and a selection patent should be filed in 2019 / 这一类新药已经进行例证，确认了3款先导化合物，2019年将申请选择的专利

PATENT 2 / 专利2

Patent **WO2014/114742** has been filed (PCT) by VFP Therapies 70% and its academic partners 30% / 专利**WO2014/114742**由VFP Therapies及其学术合作伙伴合作申请，各占70%和30%

It covers a large family of drug candidates which could be marketed in future to compete commercial drugs like Aricept® / 该专利包含一大类的候选药物，这些药物未来可能问世并与Exelon®这样的商业药物展开竞争

The PCT procedure has been launched in January 2015, the patent has been granted in United States of America, Canada and Europe / 专利合作条约程序已在2015年1月启动，该专利已在美国、加拿大和欧洲获得



ALZEX PIPELINE

ALZEX 产品管线



	Hit identification 命中识别	Lead search & optimization 领导搜索和优化	Pharmacology & preliminary toxicology 药理学和初步毒理学	Pre-clinical development 临床前开发	Phase I 一期
Patent 1 Prodrug of AChE inhibitor 专利1 AChE抑制剂的前体药物		Alzheimer / 阿尔茨海默病			
Patent 2 Prodrug of AChE inhibitor 专利2 AChE抑制剂的前体药物		Alzheimer / 阿尔茨海默病			
New small molecules Prodrug of BChE inhibitor 新的小分子 BChE抑制剂的前体药物		Alzheimer / 阿尔茨海默病			
New small molecules Selective kinase inhibitor 新的小分子 选择性激酶抑制剂		Alzheimer / 阿尔茨海默病			
		Down syndrome / 唐氏症			
New small molecules Prodrug of MTDL 新的小分子 MTDL的前体药物		Autistic disorders / 自闭症			
		Schizophrenia / 精神分裂症			
New small molecules Prodrug of MTDL 新的小分子 MTDL的前体药物		Alzheimer / 阿尔茨海默病			

VFP THERAPIES: SCIENTIFIC R&D MANAGEMENT

VFP THERAPIES: 科学研发管理团队



Dr. Francis Marsais, Founder & CEO
Francis Marsais博士，创始人兼首席执行官
Ph.D. in Organic Chemistry
有机化学博士

Former director of an important academic research group within the Institut de Recherche en Chimie Organique Fine (13 years) / 有机化学研究所内一个重要的学术研究组织的前主任（13年）
Former director in charge of partnerships at the Institut National des Sciences Appliquées (5 years) / 国家应用科学院负责合作项目的前主任（5年）
Author of over 130 international papers and holds 5 patents / 发表国际论文130余篇，拥有5项专利

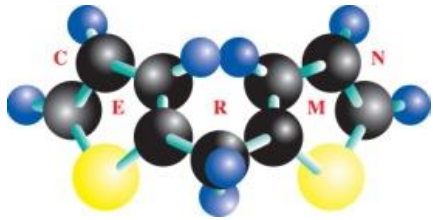


Dr. Vincent Gembus, CSO
Vincent Gembus博士，首席科学官
Ph.D. in Organic Chemistry
有机化学博士

Manager of various R&D project in medicinal chemistry on behalf of pharmaceutical partners / 代表医药合作伙伴管理医药化学领域的各类研发项目
Author of high level international papers / 发表多篇高水平国际论文
Excellent experience of the pharmaceutical development & Key leader of the R&D team / 拥有极为丰富的作为医药研发团队主要负责人的经验

FRENCH SCIENTIFIC, TECHNOLOGICAL & FINANCIAL PARTNERS

法国科学、技术与金融合作伙伴



SCIENTIFIC AND BUSINESS PROJECTS

科学与商业项目

- ❖ 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) / 凭借着在法国十多年的研究优势，VFP Therapies的疗法带来了一种创新的反应，以最大限度地减少药物的有害副作用，并克服穿越血脑屏障问题。已完成的研究已经证明了这一概念最初在体外和体内模型的应用（大鼠和小鼠）
- ❖ The R&D target = achievement of preclinical assays and successful phase 1 trials / 研发目标=完成临床前试验并成功进行一期试验
- ❖ 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 / 如果获得积极的试验结果，我们就可以与制药公司商谈合作，要么代理我们的产品，要么协商共同开发制药公司自己的阿尔茨海默症药物或者其他中枢神经系统疾病治疗药物
- ❖ The current ALZEX short and mid-term expectations: / 当前的ALZEX的短期和中期预期：
 - Fulfill an ongoing fundraising round (over \$ 10 million): contact ALZEX / 完成正在进行的一轮融资(超过1000万美元): 联系ALZEX
 - Negotiate a Patent Operating Licence (upfront payment & milestones): contact VFP Therapies / 洽谈专利运营许可证(预付款和里程碑): 联系VFP Therapies
 - Find a pharmaceutical group to build a sustainable partnership: contact VFP Therapies / 找到一个制药集团并建立可持续发展的伙伴关系: 联系VFP Therapies

CAPITAL STRUCTURE

资本结构

Current Offering / 当前发行

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

第一轮: \$2,000,000, 每股\$0.25, 每份认股权证\$0.30 (800万股)

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

第二轮: \$3,000,000, 每股\$0.50, 每份认股权证\$0.75 (600万股)

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

首次公开发行前融资 (2019年2月) - \$5,000,000, 每股\$1.00, 每份认股权证\$1.50 (500万股)

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

发行股数:(首次公开募股前) - 19,000,000

Warrants: 19,000,000

认股权证: 19,000,000

Fully Diluted: 38,000,000

完全摊薄后股数: 38,000,000

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