



**Severe Orphan
Lung Diseases**

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&

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Chairman

Corporate Presentation

February 2013

OSE Pharma Investment Thesis

Substantial late stage clinical assets:

Phase 3 study for advanced lung cancer (NSCLC): targeted cancer immune therapy

100M\$ Epimmune investment from R&D to the completed Phase IIb

Phase 2 study for Cystic Fibrosis: re-profiling existing drug with safety package

Experienced team with solid track records

Emile Loria, M.D., Former Epimmune Pres & CEO

Dominique Costantini, M.D., Former BioAlliance founder & CEO

More than 100M€ raised publicly with approved EU/US products

OSE Pharma Investment Thesis

1st round to be raised: 5M€ plus commitment to 10% IPO

GMP Material for phase 3

FDA /EMA Protocols acceptance

Orphan designations

IPO preparation in 12-18 Months

2nd round to be raised: 20M€ through public market

Clinical Phase 3 execution for Lung cancer (NSCLC : Non Small Cell Lung Cancer)

Clinical Phase 2 execution for Cystic Fibrosis («mucoviscidose» a genetic disorder)

OSE Pharma Market opportunity : €1.4B

OSE 2101 targeted cancer immune therapy:

EUROPE HLA A2 positive NSCLC: 123 000 Pts

Peak Market share 15% : 18 450 Pts (cost 45 K€ to 50K€)

OSE 2101 Market Estimate **€1B**

OSE1101: molecule for Cystic Fibrosis

EU & US Cystic Fibrosis Pts: 65 000 Pts

Peak Market share 15%: 9770 Pts (cost 35K€ to 50K€)

OSE1101 Market Estimate: **400M€**

OSE Pharma assets in late stage products

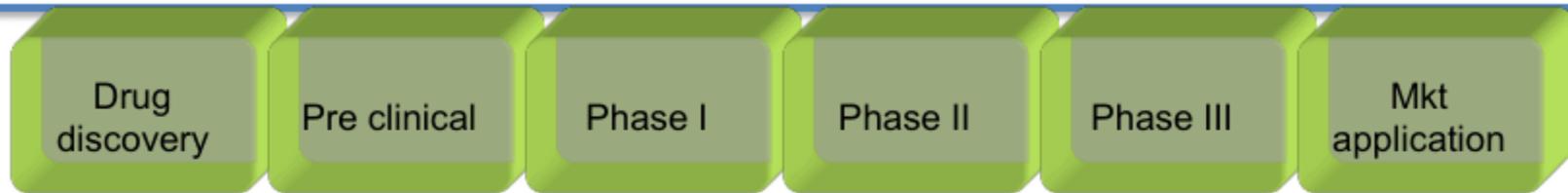
OSE 2101 Targeted immunotherapy assets:(10 years investments / \$100M)

1. R&D Epitopes algorithms definition and selection
2. Original combination of epitopes and analogs (granted PI)
3. Solid Know-how (former Epimmune team: bio batches & GMP site)
4. Up to Phase IIb positive results under US IND
5. Phase II status in colon cancer

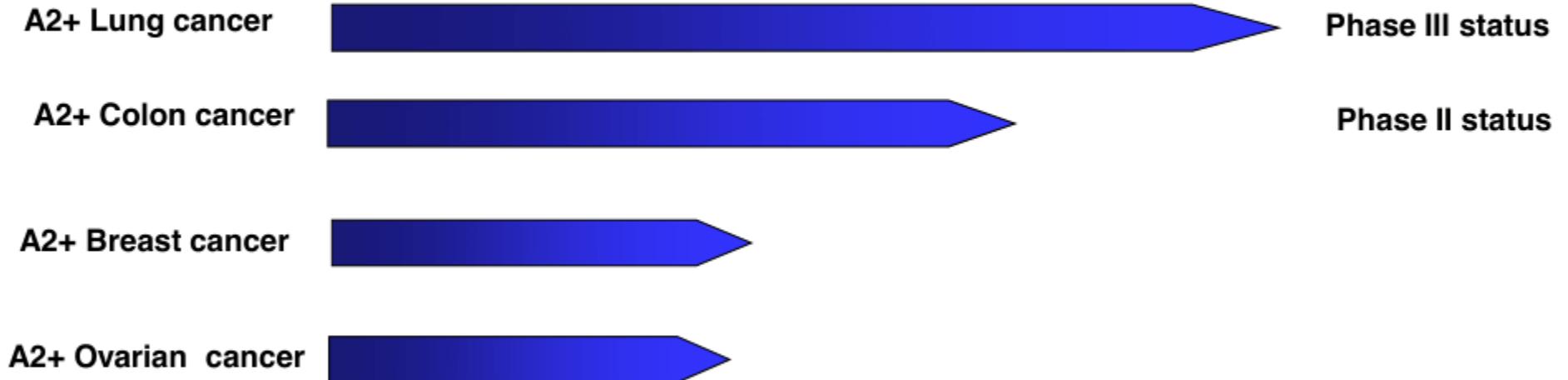
OSE1101 reprofiling a molecule previously marketed

1. safety package
2. H4R agonist patent in the US
3. Cystic Fibrosis Patent filed in 2012

OSE Pharma advanced pipeline



OSE2101: targeted Cancer Immune Therapy



OSE1101: H4R agonist





**OSE 2101 PHASE 3
OPPORTUNITY
in
advanced NSCLC**

NSCLC: New therapies critically needed

NSCLC treatments insufficiently effective: 5-year survival at 4% for patients with distant disease (Horner et al. 2009)

Active cancer Immunotherapy today: promising new treatments in Phase III

Cancer vaccines targeting only one Tumoral antigen : i.e. MAGE or MUC in clinical development in first line (or maintenance) treatment in advanced NSCLC

Ipilimumab Yervoy[®] acting on CTLA4 checkpoint (increasing T cell responses) and registered in melanoma / New anti PD1 acting on PD1 checkpoint.

NSCLC: New therapies critically needed

NSCLC treatments insufficiently effective: 5-year survival at 4% for patients with distant disease (Horner et al. 2009)

Current therapies registered for advanced NSCLC stages:

Stable disease after 1st line chemotherapy + platinum:

survival ~12 months; 1 year survival at 50% (i.e. erlotinib, perimetrexed, gemcitabine, docetaxel..)

Aggressive disease after first line failure:

survival ~8 months; 1 year survival at 33% (2nd or 3rd line) TKI or chemotherapy (i.e erlotinib, docetaxel, perimetrexed..)

ALK Inhibitors Crizotinib Xalkory[®] registered in ALK+ NSCLC pts (3-5% NSCLC pts)

OSE 2101:Phase III Protocol & Objectives

HLA A2 NSCLC population, open, randomized, multi-center comparative study: 500pts

- Versus reference drug (Treatment of Physician's Choice) after at least failure of first line chemotherapy in locally advanced IIIb or metastatic IV NSCLC patients
- Exclusion criteria:
 - specific mutations EGFR – ALK
- Primary Endpoint: Overall Survival (OS)
One year survival rate
- Secondary Endpoints: Safety, PFS, QOL

OSE 2101:Principal Investigators

- **John Nemunaitis, M.D.** Oncology Mary Crowley center, Dallas
 - Principal investigator for Phase II; expertise in numerous cancer vaccine trials

- **Benjamin Besse , M.D,** Oncology Gustave Roussy center, Paris
 - Cancer expertise in numerous cancer vaccine trials; Expert in Lung cancers (ESMO)

OSE2101 Product Manufacturing

Epitopes	Antigens
LLTFWNPPV	CEA.24V9
YLSGADLNL	CEA.605D6
IMIGHLVGV	CEA.691H5
KVFGSLAFV	HER2.369V2V9
RLQETELV	HER2.689
YLQLVFGIEV	MAGE2.157
KVAEIVHFL	MAGE3.112I5
KLBPVQLWV	p53.139L2B3
SMPPPGTRV	p53.149M2
aKXVAAWTLKAAa	Thelper PADRE

10 HLA A2 multi-epitopes targeting 5 Tumors Antigens expressed in NSCLC

Mineral oil adjuvant
(Montanide[®]ISA 51)

EP2101

1. SINGLE VIAL (5MG/ML)
2. 3 year stability of peptide emulsion
3. Manufacturing: Althea, San Diego
4. Subcutaneous Injection

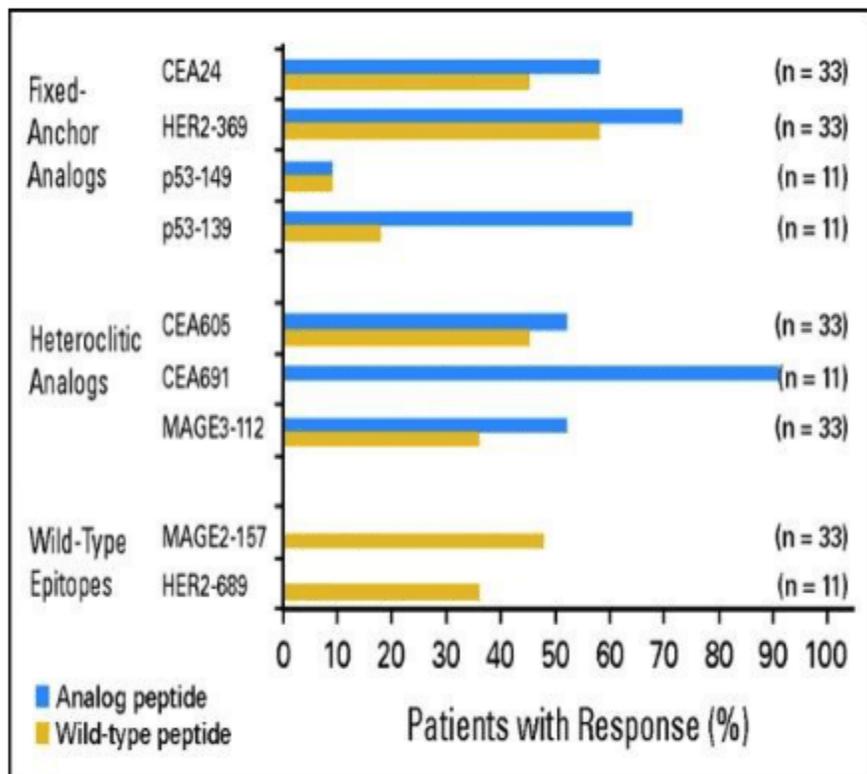
OSE 2101 Phase II positive results

Stage III-b and IV NSCLC Patients

Design: Open multicenter study : 135 patients

- 64 HLA A2 positive patients received OSE2101(stage IIIb :21; Stage IV: 43)
- 71 HLA A2 negative concurrent control patients (one year survival follow up)
- Inclusion criteria - **Stage III-b and IV NSCLC Patients**
 - ECOG status of ≤ 1 ; At least 4 weeks from last chemotherapeutic regimen
 - no limit in previous lines treatment (36% received more than 3 previous lines)
 - 6 subcutaneous doses at 3 week intervals, maintenance doses at 3 month intervals
- Immune monitoring (made for 5 of the 10 epitopes)
 - At baseline, week 9, weeks 18, 22, 30, and months 9 and 12
- Primary Endpoints: Safety and overall survival
- Secondary Endpoints: Progression-free survival, immunogenicity

Phase II Immune Responses and Survival



*M. Barve et al JCO 2008 and J. Clin Oncol 26: 2008 (May 20 suppl; abst 8057)

- **91%** (30/33) monitored for CTL showed positive responses to 1 or more, 64% to at least 3 epitopes
- **Significant relationship of epitope response level to survival of treated patients (Janus review 2012)**

Low: 0-1-epitopes: 406 ± 58 days of survival (n=5; 95% CI for mean 292 -520)*

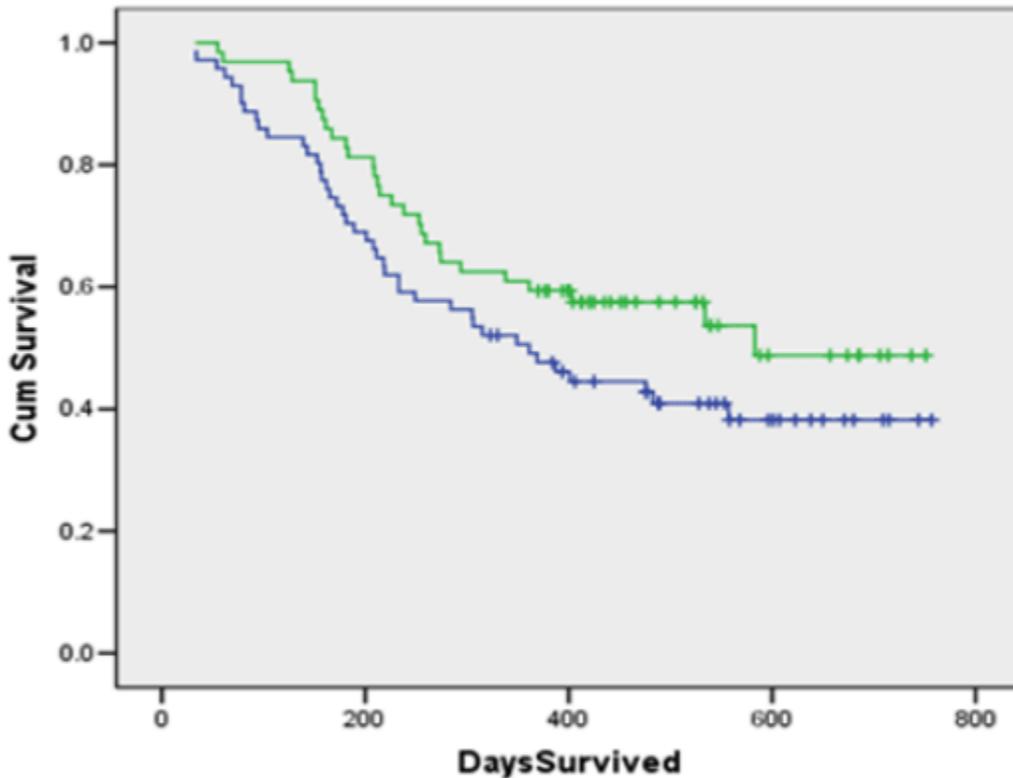
Medium: 2 to 3-epitopes : 778 ± 72 days of survival (n=15; 95% CI for mean 637 -919) *

High: 4 to 5-epitopes: 875 ± 67 days of survival (n=13; 95%CI for mean 743- 1007) *

In all categories stated above: p < .001

Phase II Overall Survival at 1 Year

Survival Functions



Received OSE2101

- No
- Yes
- No-censored
- Yes-censored

135 patients

Green = OSE2101 Treated =64 (29 deaths)

Blue = Control =71 (42 deaths)

A2 negative parallel selection

One-year survival: p=0.063

Control A2 negative patients= 49%

better prognosis established- Nagata 2009

Treated A2 positive patients= 59%

Median survival (days):p 0.086

Control patients= 361 ± 59

Treated patients= 583 ± 138

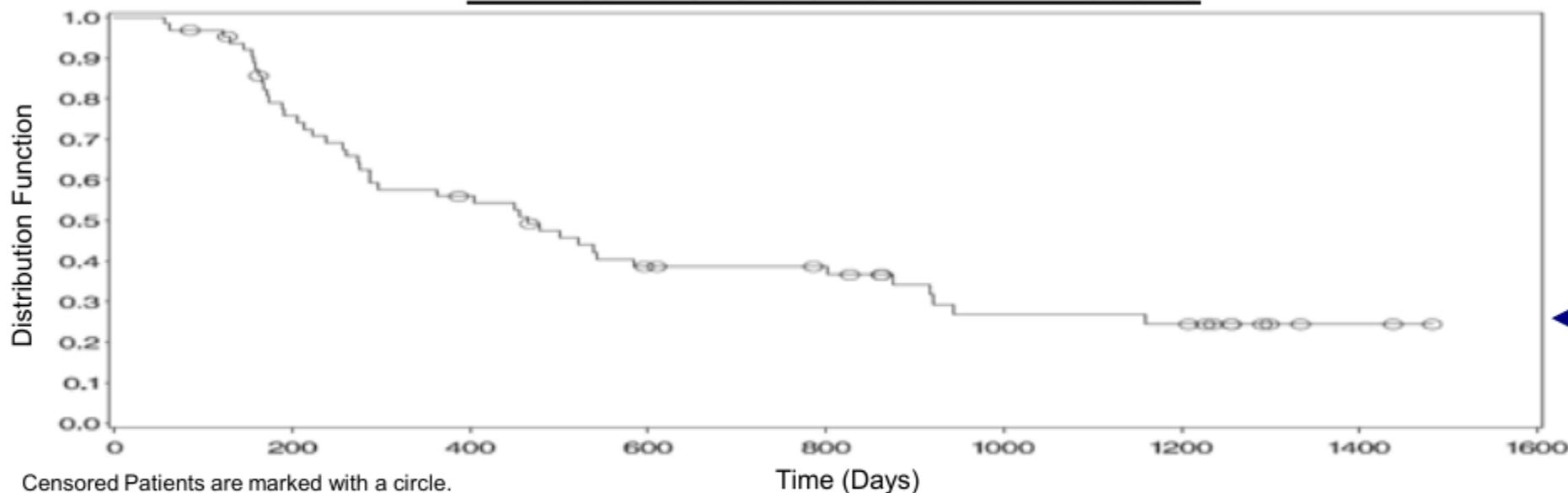
7.5 months of difference

*M Barve et al; J Clin Oncol 26: 2008 (May 20 suppl; abstr 8057); J Neimunatis et al; International Society for Biological therapy of cancer 2007 Abs :phase II trial of a 10- epitope CTL vaccine in metastatic NSCLC



Phase II Overall Survival at 4 Years

K – M Curve of Overall Survival All Patients



Paient Group	N	One Year Survival Estimate (95% CI)	Two Year Survival Estimate (95% CI)	Three Year Survival Estimate (95% CI)
All	64	56% (44-68)	39% (26-51)	27% (15-39)
Stage IIIb	21	74% (54-94)	48% (25-70)	24% (2-46)
Stage IV	43	48% (33-63)	35% (20-50)	28% (14-43)

Stage IV
67% →

OSE 2101 Positive Phase II Conclusions

- Strong clinical efficacy signal observed in locally advanced or metastatic NSCLC patients: median survival better than 17 months
- **89%** of patients demonstrated stable disease
- 25% overall long term survival rate at 4 years
- 85% of patients tested presented an immune response
 - A minimum of 2 epitopes; n=33 for the 5 epitopes tested
- Longer survival shown in patients achieving response to 2 or more epitopes
 - $P < .001$, n=33 for 5 epitopes tested
- Primary adverse effect: injection site reaction

OSE 2101 Milestones & Use of Proceeds

OSE 2101 targeted cancer immune therapy with positive phase II:
Phase III in advanced HLA A2+ NSCLC pts:
global costs: €23M (including team and G&A)

12/18 months Milestones: Total 4M€

- Orphan status
- FDA/ EMA Phase III Agencies green lights
- Scale up / GMP Biobatches

OSE 2101 Timelines & Costs

<u>Subject</u>	<u>Date</u>	<u>€19.3M</u>
▪ Orphan status for NSCLC A2 population :	Q1 2013	
▪ GMP Material Phase 3 FDA/EMA acceptance :	2013	€4M
▪ Pivotal clinical program :	2014-2016	€15.3M
▪ Phase 3 results (one year OS rates)	2016 -2017	

OSE 2101 Intellectual property

OSE 2101 key patent: EP2101 ten epitopes describing HLA A2 Epitopes and or **analogs** combinations from different Tumor Associated Antigens (HER2/neu, CEA, MAGE2; MAGE3; p 53) plus synergy obtained by the original combination :

- **Granted in Europe** (PCT application WO2004094454) filed in April 2004 - protection until 2024
- Other multi-epitopes patents are using modified epitopes: epitopes identification, selection and modification based on immunogenicity results and HLA binding for immune therapy and constitute a barrier to entry
- New patents in the course of development

Know-how: manufacturing of a multi-epitopes composition; process and methods of preparation of 10 peptides combination

OSE 2101 Business Strategy

Partnering opportunities in non core territories

Major Pharma deal or sale of assets post phase 3

Market Opportunity: €1B



**OSE 1101 PHASE 2
OPPORTUNITY
in
Cystic Fibrosis - CF**

OSE 1101 CF Phase II independent product

OSE1101 (tritoqualine) was selected

- As indicated in severe lung disease: Cystic Fibrosis
- Cystic Fibrosis qualified for Orphan designation
- independent development risk
- Same regulatory and development team as EP2101
- Molecule with a proven safety profile previously marketed in Europe
- Original new anti-inflammatory properties for a CF application

CF: New therapies critically needed

With current treatment strategies, 80% of patients should reach adulthood, Cystic Fibrosis remains a life-limiting disease (median survival : 36.9 years)

OSE1101 is a new anti-inflammatory molecule (H4R agonist/IL8 decrease)

Maintaining lung function

Mucolytic agents (i.e. dornase alfa ,Pulmozyme®)

Nebulized, inhaled, oral, or intravenous antibiotics

Bronchodilators

Anti-inflammatory agents

Current new therapies registered for CF

Agents acting to reverse chloride transport abnormalities (Kalydeco , ivacaftor®) on specific mutation (4% of CF /annual cost 294 000\$)

hydrating the airway surface : Inhaled mannitol Bronchitol® (EU Australia)

OSE 1101 in Cystic Fibrosis

- **OSE1101** as a new H4R agonist & histamine modulator
- Role on histamine level and interleukin release as IL8
- IL8 is a potent chemo-attractant playing a key pro-inflammatory role in stimulating conditions (bacterial and viral infections) or in chronic conditions related to CFTR gene in CF patients
- **OSE1101** is an innovative potent anti-Inflammatory compound targeting H4R expressed in CF and decreasing IL8 release
- **OSE1101** protects mice against bronchospasm induced by two types of provocation tests (in vivo Ovabulmine/TLR 7).
- **OSE1191** induced rise in breath-flow in human intra nasal provocation tests (n = 49-600mg/d - 5 days - Gastpar, H. and Sauer, P.H.)

OSE 1101 proven safety Profile

- **OSE1101** previously marketed for allergic disorders as a histidine decarboxylase inhibitor: histamine modulator
 - Decreases the tissue formation of endogen histamine from histidine
- Marketed internationally since 1960 (Chiesi – Novartis consumer health) for the treatment of various allergic conditions
 - 300 to 900mg/d with no obvious side effects
 - Clinical dossier based on extensive prior human use and clinical efficacy on nasal or allergic symptomatology

OSE 1101 Milestones & Use of Proceeds

OSE1101 H4R agonist for CF Patients reprofiled molecule

Phase II in CF pts: total €3.8M (\$5M)

PK/PD/dose efficacy and safety in young CF patients (age >10)
endpoint : FEV1 improvement vs placebo (follow up 24 / 48 weeks)

12/18 months Milestones: Total 1M€

- CF in vivo results : P Barbry, IPMC Director (Sophia Antipolis)
- Orphan status
- FDA/ EMA Phase II Agencies green lights
- GMP Biobatches

OSE 1101 Timelines & Costs

	<u>Date</u>	<u>Capital €3.8M</u>
▪ Orphan status for CF population :	Q1 2013	
▪ Scale up and bio batches stability :	2013	€0.8M
▪ Phase II clinical program :	2013-2015	€3M
▪ Phase 2 results:	2015	

OSE 1101 Intellectual Property

- *H4 Receptor agonist, US Patent # 8,207,188 - E Loria, M Nicolaou..* Granted in the US until 2029
- Cystic Fibrosis application: April 2012, OSE Pharma EP 12305487.6 opening International protection until 2032
- New patent in the course of development
- EU US Orphan status protection to be filed in 2013

OSE1101 Business Strategy

Partnering opportunities to explore

Major Pharma deal or sale of assets post phase 2

US & EU Market Opportunity: €400M

Management Team

Dominique Costantini, M.D. Pres. & CEO

- Former Founder and CEO BioAlliance Pharma (1997-2011, publicly traded on the EuroNext)
- More than €100M raised, three products approved EU/US supportive care and oncology
- Management of drug development and launches (HMR – Sanofi) -M.D, Immunology

David Dellamonica, COO

- Theralpha founder and CEO, TxCells VP BD Biotech
- Sanofi consultant, Patient Solutions i.e. Colitis foundation & PCSK9
- International Marketing experiences Lilly; Ogilvy- ESG Lyon, MBA Switzerland

Elisabeth Peyraube, CFO

- 15 years experience in international companies of which 5 years in the US.
- CFO Metaboli-. CFO ADP GlobalView- USA: SFG, Ubisoft
- Arthur Andersen Auditor.- EDHEC accounting and finance

Consultants and Advisors

Jean Bernard Lepecq, Ph.D. Palo Alto

- Developed Taxotere for Aventis
- Expertise in cancer vaccines

Alex Sette, Ph.D. La Jolla

- Former Epimmune CSO
- Developed algorithm programs at Epimmune and currently at La Jolla Institute for Allergy

Alain Chatelin, M.D. pneumologist -Altius - Paris

- Consultant to the Pharma and Biotech
- Developed products in infectiology, oncology, respiratory field. (HMR) .Altius Pharma CEO
- Contributed to orphan status for both OSE products and will be involved in the phase III coordination program

Jim Carter, Ph. D. Regulatory compliance Inc Las Vegas

- US FDA OSE representative, Consultant to the Pharma and Biotech (IND/registration/API dossier). Large FDA regulatory experiences and network

Mike Nicolaou, Ph.D. San Diego

- Former Epimmune Director of Manufacturing
- Expertise in formulation, manufacturing, QA/QC, bioassays (Amylin, Yasoo Health)

Les Walker, PhD; San Diego

- Former Epimmune Director of process,
- EP-2101 batches for Phase I/I and phase II
- Expertise in vaccine and peptide manufacturing

Fred Bancroft, San Diego

- QA/regulatory (Amylin)

Steve Reich, M.D Oncologist. San Diego

- Consultant Pharma and Biotech,
- involved in EP-2101 phase I and II designs
- Contributing to phase III protocol.

Board of Directors

Emile Loria, M.D., Chairman

- Former President & CEO of Epimmune (Nasdaq:EPMN), Science and Business expertise
- Biotech and Pharma companies (Biovector Therapeutics, Medical Synergy/Cygnus, Sanofi, Ciba-Geigy)

Dominique Costantini, M.D., CEO

- Founder and CEO of BioAlliance, more than 100M€ raised and products approved in EU/US
- HMR, Roussel

Guy Chatelain

- Attorney at Law, partner Mentha & Associés
- Geneva and Swiss Barr association, Geneva association of Business Law

Walter Flamenbaum, M.D.

- 40 years of healthcare experience in innovation and investments , Paul Capital partner emeritus, Professor of medicine at Mount Sinai University, MD at Columbia University

Jean Theron

- Founder and Managing Director of JT.Pharma International Consulting
- Former President Hoechst Marion Roussel France,
- CEO of Hoechst Roussel Diamant, Lutsia, Hoechst Behring

Business models and Comparables

- **Biovex / Amgen acquisition 2011: \$425 million cash up to \$575 million in additional payments**
 - oncolytic vaccine in Phase 3, melanoma/ H&N cancers
- **Immatics 108M€ Invested in 3 rounds**
 - natural peptides from primary tumour tissues/ Phase III in renal cell carcinoma-phase II in colon cancer
- **Novartis -Transgene Option : 995M\$ deal in 2010**
 - Muc tumor antigen/ IL2 recombinant Virus in Phase III - NSCLC/ first line Treatment
 - Deal with Novartis 10M\$ upfront in phase IIb /III
- **AB Sciences (594M€ Euronext)**
 - Masitinib at registration stage in Pancreatic cancer + other indications

Value proposition after first private placement

Breakthrough products addressing €1.4B markets

NSCLC leading cause of cancer mortality/ CF is killing before 40

Milestones targeted after 5M€ 1st round

Increasing value in 12/18 months:

OSE 2101 targeted cancer immune therapy phase III in advanced HLA A2+ NSCLC

OSE 1101 H4R agonist Phase II in CF pts

- **Orphan** status for both opportunities
- FDA/EMA protocol acceptance and partnering opportunities
- GMP materials

Limited risk due to late stage clinical drugs (Phase 3 and Phase 2)

Next step and exit strategy

IPO feasible with these assets
and management expertise
next 12-18 months

5 IPO done in 2012 with far less advanced portfolio

Opportunity as Pre IPO round at attractive valuation

Pharma deal/ sale of the assets after clinical data



Contacts



**severe Orphan
lung diseases**

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