

**Estimated price\*:** €15.25

Share price (€) 7.56

(as of Mar. 16<sup>th</sup>, 2016)

High/Low (€) 8.59/5.70

(since Jan. 1<sup>st</sup>, 2016)

Market Cap. (€M) 76.0

(as of Mar. 16<sup>th</sup>, 2016)\*

Estimated Net Cash 16.6

(€M)

Estimated Market Cap. 153.2

(€M)

Number of shares (M) 10.05

Estimated price (€) 15.25

3-month average daily 12,000

volume

Free Float 29.7%

\*Does not include the value of Effimune

*Euronext since Jan. 1<sup>st</sup>, 2016*

**OSE Pharma** -10.7%

**Alys France\*** -15.6%

**Next Biotech** -18.5%

**CAC Healthcare.** -7.4%

**CAC 40** -3.75%

**CAC Small** -4.67%

\* Index of French smallcaps (less than €1B market capitalization at time of inclusion) in the healthcare and life sciences sector, listed on Euronext Paris.

See <http://www.aurgalys.com/aurgalys-indices>

## OSE Pharma and Effimune merge to become a leader in immunotherapy

OSE Pharma announced its proposed merger with privately-held biotechnology company Effimune, which specializes in the development of treatments for auto-immune diseases and for cancer. The combined entity, to be named OSE Immunotherapeutics, will have a well-balanced pipeline of drug candidates whose mechanism of action relies on the activation and/or modulation of the immune system, giving the new company, a strong position in immunotherapy. The lead programs of OSE Immunotherapeutics, whose main strategy will remain immuno-oncology, would include OSE Pharma's Tedopi currently in Phase III trial in Europe and the United States, for the treatment of NSCLC; and Effimune's FR104, a drug candidate for Rheumatoid Arthritis. Janssen Pharmaceuticals (J&J group), is expected to exercise an option to license FR104 in H2-2016, to pursue the development of the drug in Phase II.

### OSE Pharma and Effimune to form OSE Immunotherapeutics by the end of Q2-2016

The merger announced by OSE Pharma and Effimune is subject to approval by the shareholders of both companies during their respective extraordinary general meetings, scheduled to take place by the end of Q2-2016. The merger is a non-cash transaction, whereby OSE Pharma will absorb Effimune. For 1 share of Effimune, shareholders of the company will receive 1.93 newly issued shares of OSE Pharma (OSE Pharma will issue approximately 4 million new shares). Effimune's shareholders would represent 29% of OSE Immunotherapeutics' capital, while OSE Pharma's shareholders would hold 71%. Dr. Dominique Costantini, CEO of OSE Pharma will be CEO of the new entity, whereas Maryvonne Hiance, CEO of Effimune will take the Vice-Presidency of OSE Immunotherapeutics' board of directors.

### A rational merger that combine two expertises: immunoactivation & immunomodulation

This merger between two companies involved in immunotherapy indicates that their respective management aims at becoming a strong player in immuno-strategies to fight diseases with strong

medical need. Immunotherapy is a huge field consisting of several therapy strategies that all use the immune system to fight diseases. Oncology has been a hot topic in recent years thanks to the successful approval of immunotherapy drugs targeting cancer. This particular field, immuno-oncology, exhibits strong promises in treating cancer effectively.

The modulation of the immune system has always been used to treat diseases caused by the immune system itself. Auto-immune diseases are caused by an over-activation of the immune system that recognizes endogenous components as exogenous. This perturbation leads to severe pathologies such as rheumatoid arthritis, multiple sclerosis or Type I diabetes. The expertise of OSE Pharma in specific activation of the immune system, and that of Effimune in the modulation of the immune system, could provide obvious synergies to conduct solid development programs in immunotherapy.

### **Effimune, immunomodulation for autoimmune diseases and oncology**

Effimune is a spin-off of the Nantes Institute of Transplantation Urology Nephrology-ITUN, created in December 2007. Effimune is a biotech company specializing in immuno-modulation for applications in transplantation, auto-immunity and cancer immunotherapy. The biotech has developed 3 programs in its pipeline, among which their lead drug candidate FR104, a CD28-antagonist, dedicated to auto-immune diseases and transplantation treatment.

Effimune has already secured a partnership with Janssen Pharmaceuticals, which is expected to exercise an option to license FR104 in H2-2016 following Phase I results. Janssen Pharmaceuticals is part of the J&J group which already owns two products for rheumatoid arthritis. One of Janssen product is an anti-interleukin 6 antibody currently in Phase III trial. The second product is a TNF-alpha inhibitor (golimumab) already marketed. With the option to license FR104, an anti-CD28, Janssen could expand its portfolio for rheumatoid arthritis with drugs relying on three therapeutic approaches (TNF-alpha, IL6, CD28). This strategy is confirmed by the recent participation of Janssen Pharmaceuticals in the Matwin consortium, a French cluster of academic laboratories and industries working together to develop and accelerate innovation. This illustrates Janssen's desire to be involved in early drug research, and reflects its strategy to detect and develop preclinical programs with strong potential.

Effimune's early stage programs include Effi-7, developed through the EFFIMab consortium, and led by Effimune. The aim of the consortium is to develop a new generation of an immune-modulatory antibody targeting the interleukin-7 receptor, for the treatment of

ulcerative colitis and acute Type T lymphoblastic leukemia. Effimune is a second generation ICI (Immune Checkpoint Inhibitor) developed in immuno-oncology. This program has clear synergies with OSE Pharma's therapeutic strategy in cancer.

### **OSE Pharma, a leader in immuno-oncology**

OSE Pharma is a major player in immuno-oncology. The company has developed Tedopi, an antigen cocktail, to treat several cancers for HLA-A2-positive patients. Tedopi is currently in Phase III trial (Atalante 1 trial) recently started to treat NSCLC patients. Results are expected in 2018 and the company has the financial visibility until the end of the Phase III trial. OSE Pharma intends to initiate other trials to develop their lead product Tedopi in other cancers and/or to combine it with an immune checkpoint inhibitor (ICI). The company is considering conducting a Phase II trial in NSCLC to assess the efficacy of Tedopi combined with an anti-PD1 or anti-PDL1. These two ICIs have demonstrated their strong potential to treat severe cancers such as melanoma or NSCLC. Therefore, the combination of Tedopi that specifically activates the immune system, with an ICI that modulates the immune system, could give promising results in light of recent studies using ICI in monotherapy or in combination.

### **OSE Immunotherapeutics, strong synergies for innovative drugs in immunotherapy**

The merger has a strong rationale because of the possible synergies between the two entities. First of all, OSE Pharma and Effimune both specialize in immunotherapy; thereby they can combine their skills, knowledge, and strategies. Moreover, the two companies could accelerate their development thanks to the complementarity of their therapeutic strategies. The new company would benefit from a diversified pipeline, giving OSE Immunotherapeutics a strong position in the immunotherapy field.

Furthermore, OSE Pharma, which specializes in oncology, could diversify its product pipeline to other therapeutic fields. For instance, Effimune's drug candidates mainly address the auto-immune disease market, for which numerous indications have no effective therapeutic solutions. The two approaches, activation and modulation of the immune system, would give OSE Immunotherapeutics, the necessary technologies to address a huge market with strong medical needs.

### **A strong and well-balanced pipeline**

The pipeline of OSE Immunotherapeutics will consist of several drug candidates at different stages of development. This strategy will help reduce the risks for OSE Immunotherapeutics which will also mitigate the associated costs.

- Tedopi is being developed for NSCLC: it is a combination of 9 neo-epitopes commonly found in NSCLC, and is given via subcutaneous injection. After immunization, the patient's immune system will be activated to specifically target cancer cells expressing at least one

of the 9 epitopes. The administration route developed by OSE Pharma, also makes Tedopi an interesting drug candidate in terms of patient compliance. **Phase III trial started Q1-2016.**

- OSE Pharma is considering the development of Tedopi for NSCLC in combination with an ICI: the company will combine a marketed anti-PD1 or anti-PDL1 such as Keytruda or Opdivo with Tedopi. The use of an anti-PD1 or anti-PDL1 over an anti-CTLA4 is explained by their better tolerance profile. As demonstrated in recent studies, the strategy consisting in combining 2 molecules acting by different pathways could result in a better efficacy and less side effects. **Phase II trial to be launched in 2017.**
- FR104 is being developed for transplantation and auto-immune diseases: it is a CD28-antagonist, a key receptor in effector T lymphocytes. These effector T lymphocytes are harmful in the case of autoimmune diseases and transplantation. At the end of 2013, a global license agreement was signed with Janssen for FR104. Janssen could exercise an option to license in the second half of 2016 to continue the development of FR104 in Phase 2 clinical trials. **Phase II-ready at the date of the merger (Q2-2016).**
- Effi-7 is being developed for transplantation and auto-immune diseases: it is a monoclonal immune-modulatory antibody targeting the CD127 receptor, (Interleukin 7 receptor), with in vivo proof of concept for several autoimmune models. **It is in the advanced preclinical stage.**
- Effi-dem is being developed in immuno-oncology: it is a second generation checkpoint inhibitor. It targets particular suppressor cells present in the tumor microenvironment. **It is in the preclinical stage.**

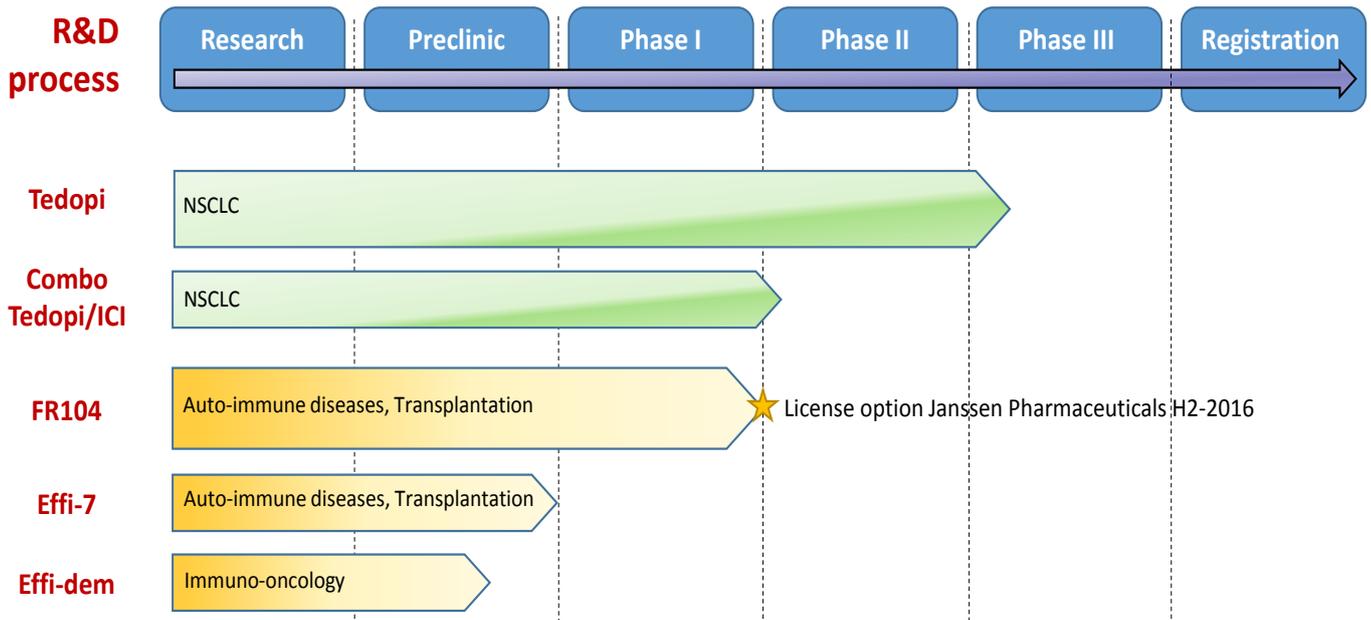


Figure 1: OSE Immunotherapeutics' pipeline after the merger is finalized (Q2-2016). Green: OSE Pharma's products, Yellow: Effimune's products.

### Valuation of OSE Pharma

Following this announcement, we decided to maintain our valuation of OSE Pharma at €15.25 per share. This target price does not include the value associated with Effimune's development programs. We will estimate the value of the new company OSE Immunotherapeutics after the merger is approved by shareholders from both companies (Q2-2016).

### Stock Performance

As with other French Biotech smallcaps, OSE Pharma was impacted by negative macroeconomic events, and more specifically, the oil crisis, the Chinese economy, and the Euro under pressure. OSE Pharma's stock lost 20.2% in January 2016, and has a -10.7% YTD performance closing at €7.56 per share on March 16<sup>th</sup>, 2016.

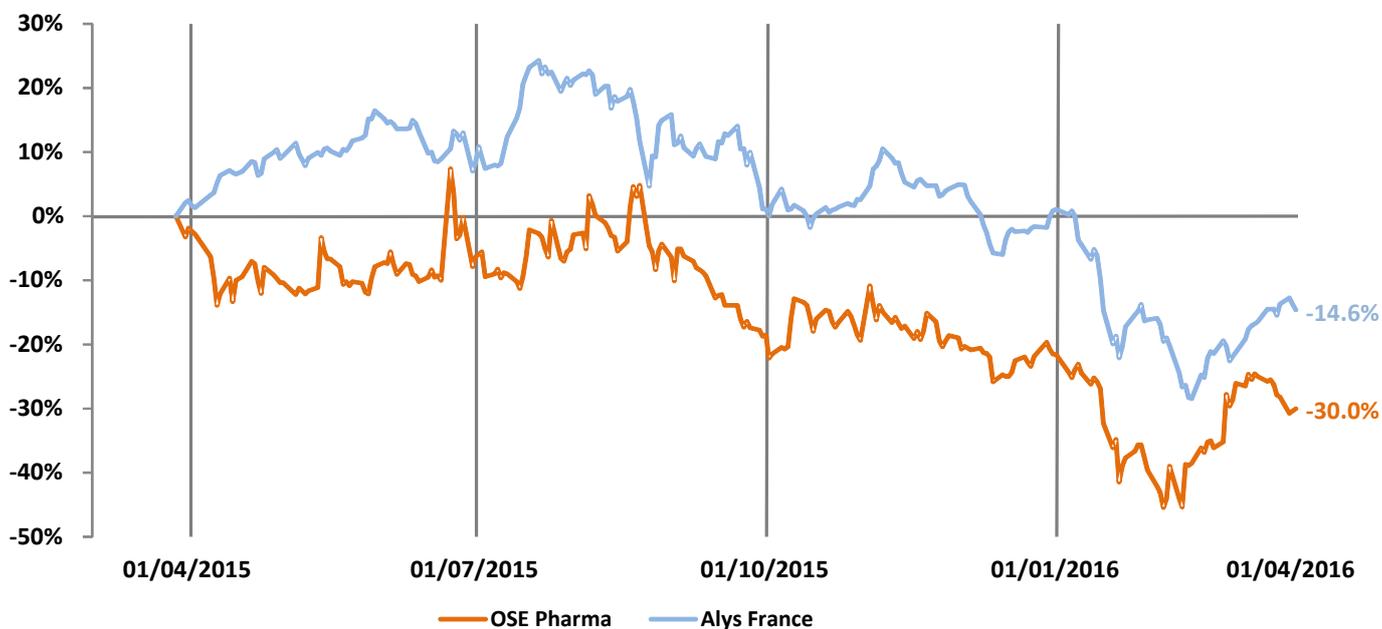


Figure 2: One-year chart dated March 16<sup>th</sup>, 2016, comparing the performance of OSE Pharma's stock with French smallcaps of the life sciences and healthcare sector (Alys France index), since the IPO of OSE Pharma (March 30<sup>th</sup>, 2015).

## Financial Data (data for OSE Pharma)

Earnings Per Shares (€)	2013	2014	2015e	2016e	2017e
EPS	-0,03	-0,36	-0,45	-0,49	-0,64

Income Statement (€M)	2013	2014	2015e	2016e	2017e
Revenues	0,0	0,0	0,0	0,0	0,0
EBIT	-0,3	-2,8	-4,2	-4,9	-6,4
<b>Net Income</b>	<b>-0,3</b>	<b>-2,8</b>	<b>-4,3</b>	<b>-4,9</b>	<b>-6,5</b>

Balance Sheet (€M)	2013	2014	2015e	2016e	2017e
Non-Current Assets	0,0	0,1	0,2	0,3	0,3
Current Assets	0,0	0,8	1,3	1,8	2,3
Cash and Cash equivalents	0,3	1,1	17,5	11,8	4,9
Total Current Assets	0,3	1,9	18,7	13,6	7,2
<b>Total Assets</b>	<b>0,3</b>	<b>2,0</b>	<b>18,9</b>	<b>13,9</b>	<b>7,5</b>

<b>Total Equity</b>	<b>-0,9</b>	<b>-0,8</b>	<b>16,1</b>	<b>11,1</b>	<b>4,7</b>
Non-Current Liabilities	1,1	0,9	0,4	0,3	0,2
Current Liabilities	0,1	1,9	2,9	2,9	3,0
<b>Total Equity and Liabilities</b>	<b>0,3</b>	<b>2,0</b>	<b>19,3</b>	<b>14,3</b>	<b>7,9</b>

Cash Flow Statement (€M)	2013	2014	2015e	2016e	2017e
Cash from operating activities	-0,2	-1,9	-2,6	-4,9	-6,7
Cash from investing activities	0,0	0,0	-0,2	-0,1	0,0
Cash from financing activities	0,3	2,8	19,1	-0,7	-0,1
<b>Change in Cash</b>	<b>0,1</b>	<b>0,8</b>	<b>16,4</b>	<b>-5,7</b>	<b>-6,8</b>

## Résumé en français

L'immunothérapie consiste à utiliser le système immunitaire comme arme pour lutter contre diverses pathologies, dont les cancers. L'avantage de cette stratégie est que l'on utilise les systèmes de défense naturels de l'organisme, sur lesquels on agit par activation ou par modulation. L'objectif est soit d'activer le système immunitaire pour lutter très spécifiquement contre des antigènes identifiés, soit à moduler le système immunitaire en agissant sur les points de contrôle qui « éteignent » le système.

Cesontcesdeuxapprochescomplémentairesqu'OSEPharma et Effimune combinent par le biais de cette fusion, annoncée le 24 février 2016. Au-delà des synergies évidentes dans les expertises, compétences et stratégies thérapeutiques, cette fusion permettra l'émergence dans le paysage boursier d'un acteur fort dans le domaine de l'immunothérapie. L'expertise reconnue d'OSE Pharma dans le domaine de l'oncologie, alliée à celle d'Effimune dans le domaine des maladies auto-immunes, permettra à ce nouvel acteur de se positionner en tant que développeur de traitements innovants dans l'immunothérapie, dans des pathologies à fort besoin médical telles que le cancer NSCLC et la polyarthrite rhumatoïde.

L'Assemblée Générale Extraordinaire qui décidera de la réalisation de cette fusion se tiendra au Q2 2016. Dans cette hypothèse, nous valoriserons cette nouvelle entreprise, laquelle deviendra OSE Immunotherapeutics, en tenant compte du portefeuille d'OSE Pharma complété de celui d'Effimune. Aujourd'hui, dans l'attente de cette fusion effective, nous maintenons notre valorisation d'OSE Pharma à 15,25€/action, compte-tenu notamment des progrès d'OSE Pharma.

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## About Aurgalys indices

Aurgalys launched on October 2013, the Alys France index measuring the performance of the 40 French smallcap companies (less than €1B of market capitalization) listed on Euronext/Alternext Paris. Three other indices also measure the performance of companies dedicated to the development of therapeutic molecules (Alys Thérapeutics), diagnostic tests (Alys Diagnostics), medical devices (Alys Medtech) and Greentech (Alys Greenetch). You can find our reports on our website at <http://www.aurgalys.com/aurgalys-indices>



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