Cyclatop: Topical cyclosporine for atopic dermatitis and psoriasis

spherium biomed

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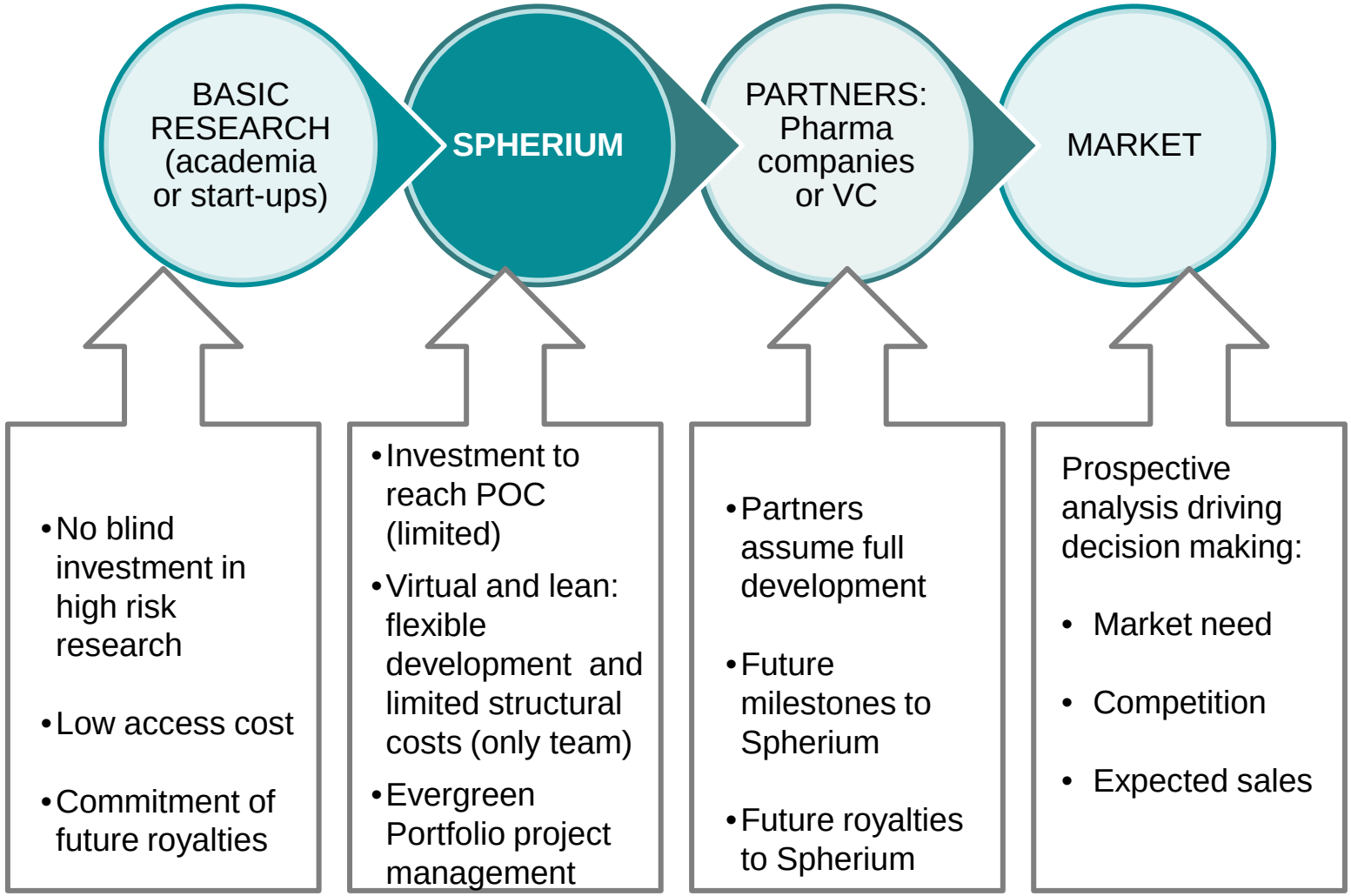
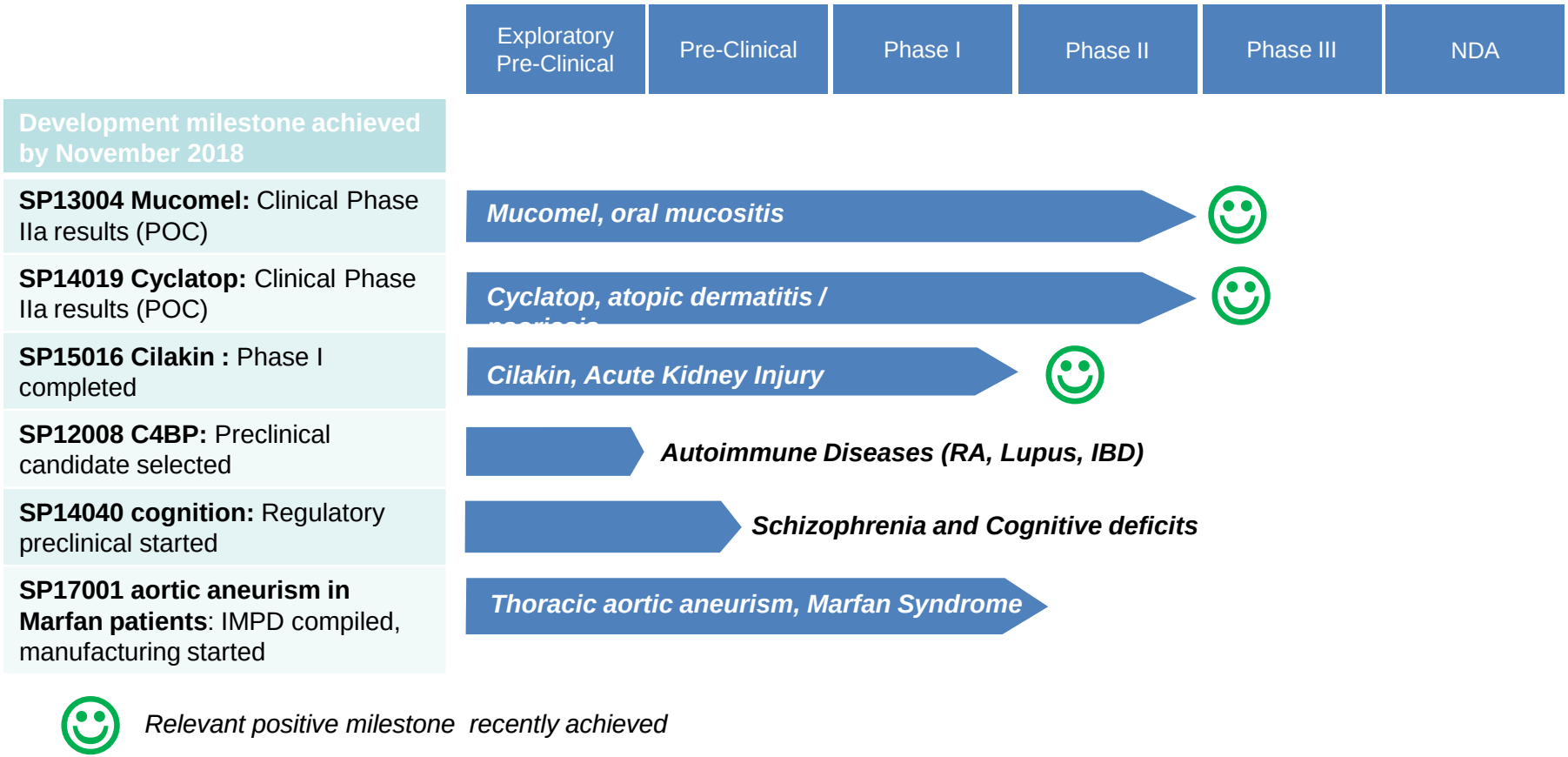
1. The Institution

- Spherium is a private, independent portfolio development company of the Ferrer Group
- focused in adding value in early stage to Proof of Concept
- continuously sourcing new innovations from academic research
- a lean virtual company
- with an experienced team with a diversified background specialized in Project Management
- developing a wide range of therapeutic opportunities with high unmet medical need (indication agnostic)

1. In the value chain…



1. Pipeline as of November 2018

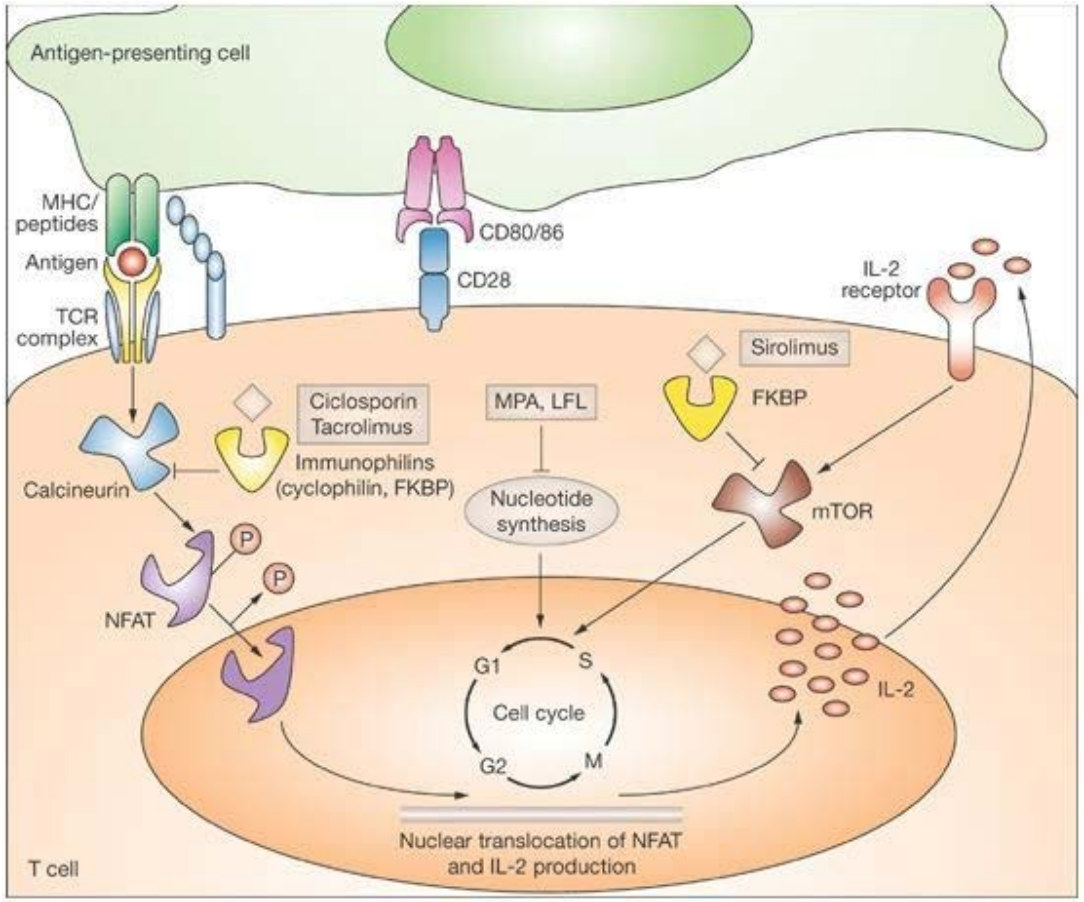


2. The Product: topical cyclosporine, 5% spray

2.a The Product: Target Indications TPP

ATTRIBUTE	TARGET
Indication	Treatment of Mild, Moderate and Severe atopic dermatitis Prevention of flare-ups of the disease Potential upside psoriasis
Target Population	>2 years-old
Efficacy	Similar to Protopic, better than Eucrisa
Safety	Better tolerated than Protopic and Elidel Minimal systemic absorption: exposure at least 100 fold lower than therapeutic dose of Neoral
Posology	Twice daily
Formulation	Scalable and stable Easier to use than creams and ointments

2.b The Product: mechanism of action



- Well known and validated mechanism: calcineurin inhibition, same as Protopic and Elidel
- Systemic cyclosporine is widely used to treat severe atopic dermatitis and psoriasis, but its use is limited by risk-benefits considerations due to nephrotoxicity

2.b The Product: experimental evidence

Non-clinical:

- Sufficient skin **penetration** with **no significant systemic** exposure
- Significant **dose-dependent efficacy**
- Good skin **safety** profile

CMC:

- Cyclosporine in a **wide range of concentrations** (from 0.1 to 10%)
- **Sprayable** oil formulation
- **Stable** formulations
- **Scalable & GMP** cost-effective production
- **Three** GMP & clinical batches 5% CsA

Clinical:

- **Positive POC Clinical Trial in Atopic Dermatitis**

2.b The Product: experimental evidence: clinical results phase IIa

- Cyclatop improves clinical signs in mild to moderate atopic dermatitis patients assessed with EASI, ADSI and IGA scales, this improvement being significantly superior to vehicle after a 4-week treatment
- The differential effect is observed already after 1 week
- This statistically significant superiority is observed in both populations analyzed (ITT and PP)
- 64% of patients revert to grade 0-1 IGA (clear or almost clear) after 4 week treatment
- The pruritus is reduced around 50% within the first week and a reduction of 3.3 points in VAS is achieved in patients with moderate pruritus (baseline VAS≥4) at end of treatment
- The systemic exposure after topical administration is very low, at least 200-fold less than the levels observed after therapeutic doses through the systemic route
- The formulation, with and without 5% cyclosporine, is well tolerated and accepted by the patients
- These results warrant further clinical development

2.c The Product: Differential features facing the market

The need of topical Cyclosporine formulations

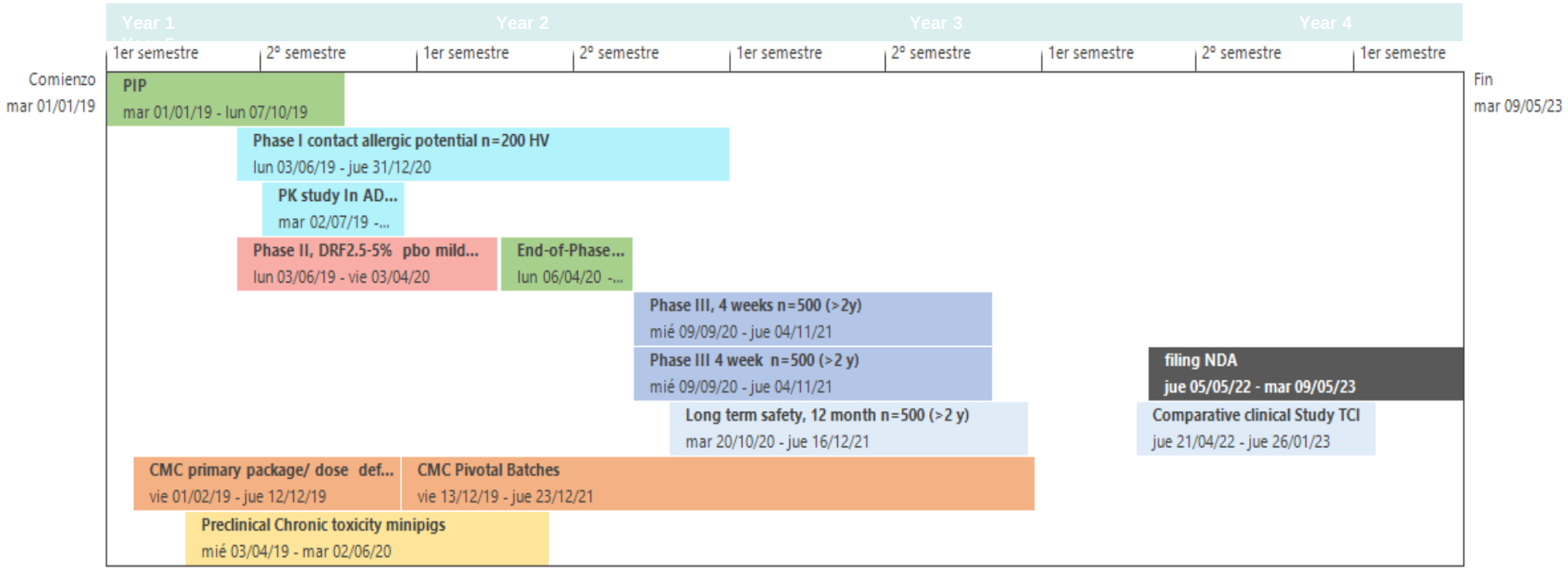
Dermatologists agree on the need of topical Cyclosporine formulations in Atopic Dermatitis and Psoriasis due to the following reasons:

- The need to **increase therapeutic tools** in Atopic Dermatitis and Psoriasis, especially in pediatric patients
- The need of **new formulations** different than creams and ointments to improve compliance
- The need to find **substitutes to topical corticosteroids,** widely rejected in pediatric patients
- The need to **reduce side effects associated to systemic use of immunosuppressants**.

Challenges in developing topical Cyclosporine so far

Cyclosporine is a potent and stable drug in skin, but technical difficulties have prevented to date the development of topical formulations of Cyclosporine due to lack of stability, production difficulties or to low penetration of Cyclosporine in the skin.

2.d The Product: current status of development



2.e The Product: IPR protection

The project is protected by 4 patent families:

- Patent filing claiming the **general formulation** system:

  "NANOPARTICLES COMPRISING ESTERS OF POLY (METHYL VINYL ETHER-CO-MALEIC ANHYDRIDE) AND USES THEREOF" nº WO 2012/140252 A1
  Priority **April 15h 2011**
  National extensions, Australia (*granted*), Canada, Europe, Hong Kong, India, Japan (*granted*), Mexico (granted), USA (*granted*).

- Patent filing claiming the **candidate Cyclosporine formulation space**:

  "CYCLOSPORINE A TOPICAL COMPOSITIONS" nº PCT/EP2017/050059.
  Priority **January 4th 2016**

- Defensive Patents filing claiming alternative Cyclosporine and Placebo formulation space:

  "CYCLOSPORINE A TOPICAL COMPOSITIONS " PCT/EP2018/067237 Priority **June 28th 2017**
  "TOPICAL COMPOSITIONS FOR THE TREATMENT OF DERMATOLOGICAL DISEASES
  PCT/EP2018/067247 Priority **June 28th 2017**

2.f Risk assessment

Below average for the development stage:

- Commercial: well established market, knowledge and appreciation of physicians of cyclosporine as therapeutic agent in the target indications
- Technical (efficacy): well established development path, well validated mechanism of action, clinical proof of concept achieved
- Technical (safety): known drug with known safety profile for systemic exposure, clinically demonstrated minimal exposure after topical administration
- Industrial (CMC): fully developed pharmaceutical form, ready for phase IIb (dose finding) and phase III

3. Partnering Opportunities

- Manufacturing rights
- Straight license
- Option to certain territories
- Co-development