



**First-in-class stem cell therapies  
to treat and prevent cancer by  
targeting cancer stem cells**

**CONFIDENTIAL**

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# VISION



To treat cancer by moving from 'Bulk' to 'Cancer Stem Cells' (CSCs) eradication



Disruptive off-the-shelf 'pan-cancer' cellular immuno-therapies against metastatic spread & relapse

Major unmet medical need in oncology of 21<sup>st</sup> Century



**TACKLING RESISTANCE AND METASTASIS**

# IPSIRIUS OPPORTUNITY

## A new frontier in Immuno-Oncology

### Ipsirius Vision

- Off-the-shelf 'Pan-cancer' stem cell-based immuno-therapies to treat and prevent cancer by targeting cancer stem cells (CSCs)

### High Unmet Medical Need

- Tackling the cause of resistance, relapse and metastasis in cancer

### Unique MoA

- Driving anti-tumor immunity against cancer embryonic-like genes and immuno-modulators that reprogram the immuno-repressive tumor micro-environment (TME)

### Development Strategy

- Pre-clinical Data / Compelling efficacy profile of first therapeutic candidate « IPVAC » in several aggressive cancer models
- Preparation of first-in-man phase I/IIb trial in NSCLC in 2023

### Strong IP

- IP portfolio covering compositions and methods of use/ worldwide exclusive license for the use of a cGMP-pluripotent stem cell line in oncology.

### Series A

- Ipsirius is raising a Series A to support the development of IPVAC in a Phase I/IIb clinical trial

# IPSIRIUS TEAM

## Highly Experienced Team in Oncology and Biotechnology



bpi**france**



**Prof. Annelise BENNACEUR**  
MD, PhD  
Hematology  
Co-founder & interim CEO  
Scientific Director  
& Strategy



**Prof. Frank GRISCELLI**  
Pharma D, PhD  
Biotherapy  
Co-founder CSO  
Scientific Director  
& Pharma



**Prof. Ali TURHAN**  
MD, PhD  
Onco-Hematology  
Co-founder CSO  
Scientific &  
Medical Director



**Aidan COURTNEY**  
Former CEO Censo  
Biotechnologies (UK)  
Corporate Development  
Manager



**Prof. Claude GRISCELLI**  
MD, Immunology  
Former CEO Inserm  
Chairman  
Non-executive Director



# Pioneers and Opinion Leaders

- **Experts in cell & gene therapies in hematology and oncology:** 25 years of management in clinical and experimental oncology
- **International expertise in pluripotent stem cells:** derivation of the first french embryonic stem cells
- > 200 iPSC lines > 500 international publications
- **Leaders of the National IPSC Infrastructure INGESTEM** ([http:// ingestem.com](http://ingestem.com)) - Investment Avenir Program
- Building the Industrial Accelerator CiTHERA 'Center for iPS Therapy' ( Genopole)
- Raising €40M public grants



## INTERNATIONAL AND EUROPEAN NETWORKS

- “Global Alliance for IPSC Therapies” ([www.global.gait](http://www.global.gait)) Board of Directors
- RESTORE ([www.restore-horizon.eu](http://www.restore-horizon.eu)): Large Scale Initiative in Europe to develop “living drugs” / ATMP (Steering Committee)

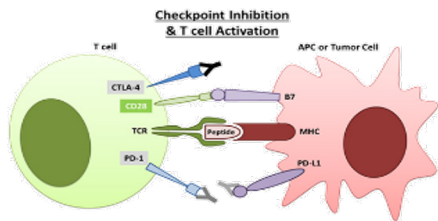


# IMMUNOTHERAPIES

## DO NOT ERADICATE CANCER STEM CELLS (CSCs)

### FDA approved Checkpoint Inhibitors (CPI)

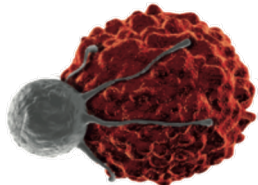
Anti PD1/PDL1, anti CTLA4



- Bristol-Myers Squibb: Opdivo (nivolumab)
- Merck & Co: Keytruda (pembrolizumab)
- Roche/Chugai: Tecentriq (atezolizumab)
- AstraZeneca: Imfinzi (durvalumab)
- Merck -Pfizer: Bavencio (avelumab)

- **65-85% Non-Responders**
- **CSC in immuno-suppressive TME**
- Side effects: autoimmune reaction

### CAR-T Cell approaches



- Novartis and Gilead ( FDA approved)
- Kite
- Juno
- Celgene
- Bluebird
- Cellular Biomedicine
- Cellectis
- Bellicum

- **Small subset of patients**
- **Restricted indications (Hematology)**
- **Do not kill CSCs (no targets)**
- Safety and toxicity concerns

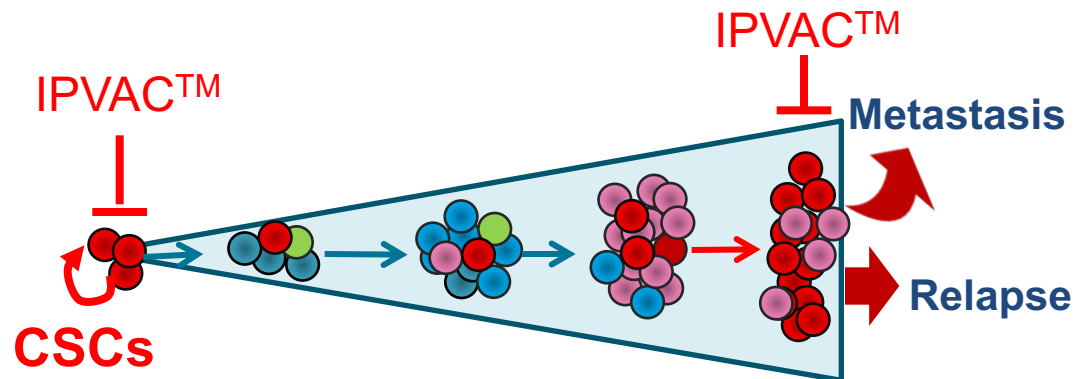
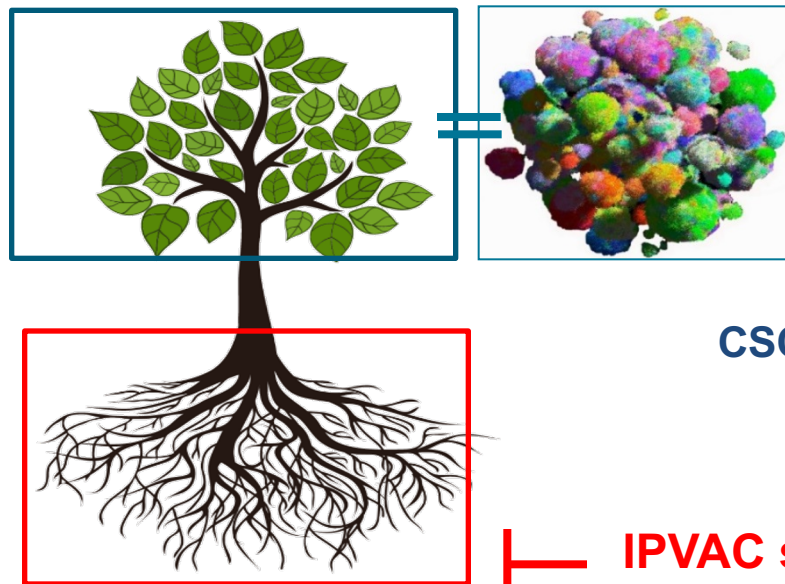
**Strong Opportunity to Overcome Resistance**

# IPSIRIUS IMMUNOTHERAPY: IPVAC™

## Moving from “Bulk” to “Cancer Stem Cells”

Conventional therapies  
Targeted therapies  
CAR-T Cell Therapies  
Cancer Vaccines

Stage I → Stage II → Stage III → Stage IV



CSCs are undifferentiated & self-renewing cells  
Replenish the tumor bulk

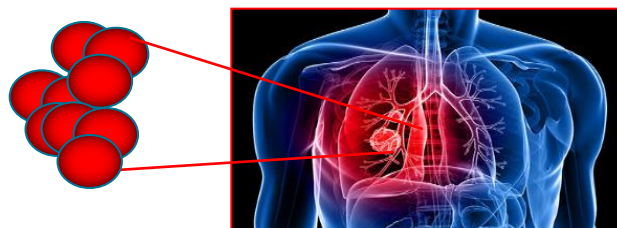
IPVAC stimulates the immune system against CSC

Primes the immune system with a wide repertoire of embryonic-like 'stemness' antigens

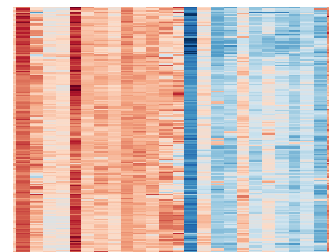
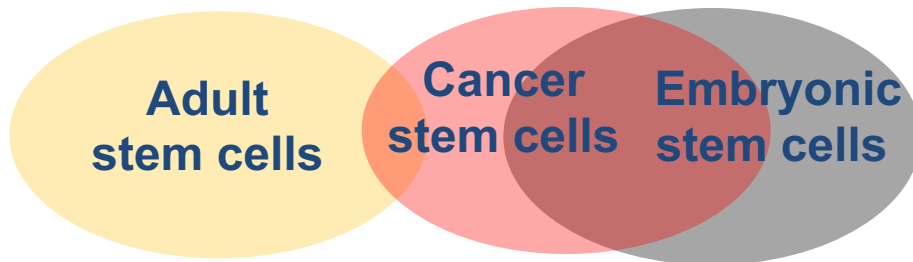
## Pluripotent Stem cells (PSCs)



## Cancer Stem Cells (CSCs)



- >1000 core PSC factors identified as Tumor Associated Antigens
- Shared with transcriptome of CSCs and NOT with normal adult stem cells



Lefort et al, Nat. Biotech 2008  
F Griscelli et al, Am. J Pathol 2012  
Balbous et al, Oncogenesis 2014  
L Tosca et al Mol.Cytogenetic 2015  
F Griscelli et al, Oncotarget 2019  
M Heront-Kishi et al, Biorxiv 2020



# IPVAC™ TECHNOLOGY PLATFORM



## IP PORTFOLIO : Proprietary technology

- ❖ IPVAC Products
- ❖ Pan-Cancer Immunotherapy
- ❖ Sub-group of cancer
- ❖ Method of manufacturing
- ❖ Therapeutic method (combo-therapy)

Allogeneic  
Pluripotent Stem  
Cells (ESC or  
iPSC)  
Master Cell Bank  
10<sup>9</sup>

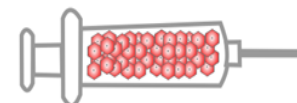
Scale up production  
in bioreactors  
Working Cell Bank  
2x10<sup>10</sup>

Pharmacological  
modification  
and  
inactivation

Fill & Finish

Cryopreserved  
vials  
Ready for  
clinical use

## IPVAC™ Products



**Committee for Advanced  
Therapies (CAT) has  
confirmed that IPVAC is a  
Somatic Cell Therapy  
Medicinal Product**



Roslin Cells

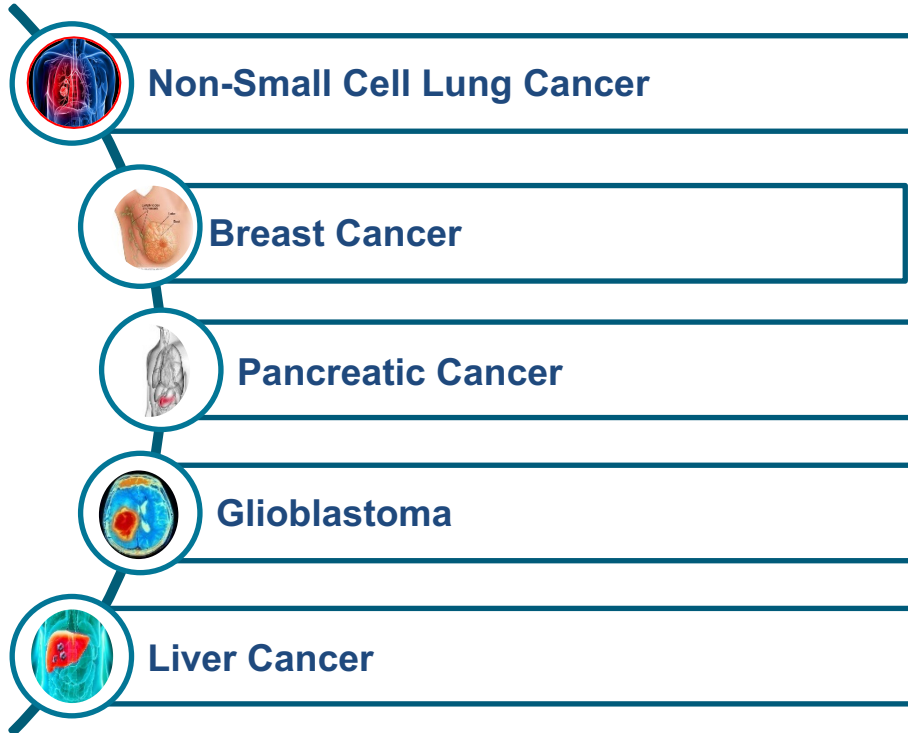


IPSIRIUS

**2020: Exclusive worldwide license of several cGMP  
pluripotent embryonic stem cell lines for cancer therapy**

# IPVAC™ PLATFORM

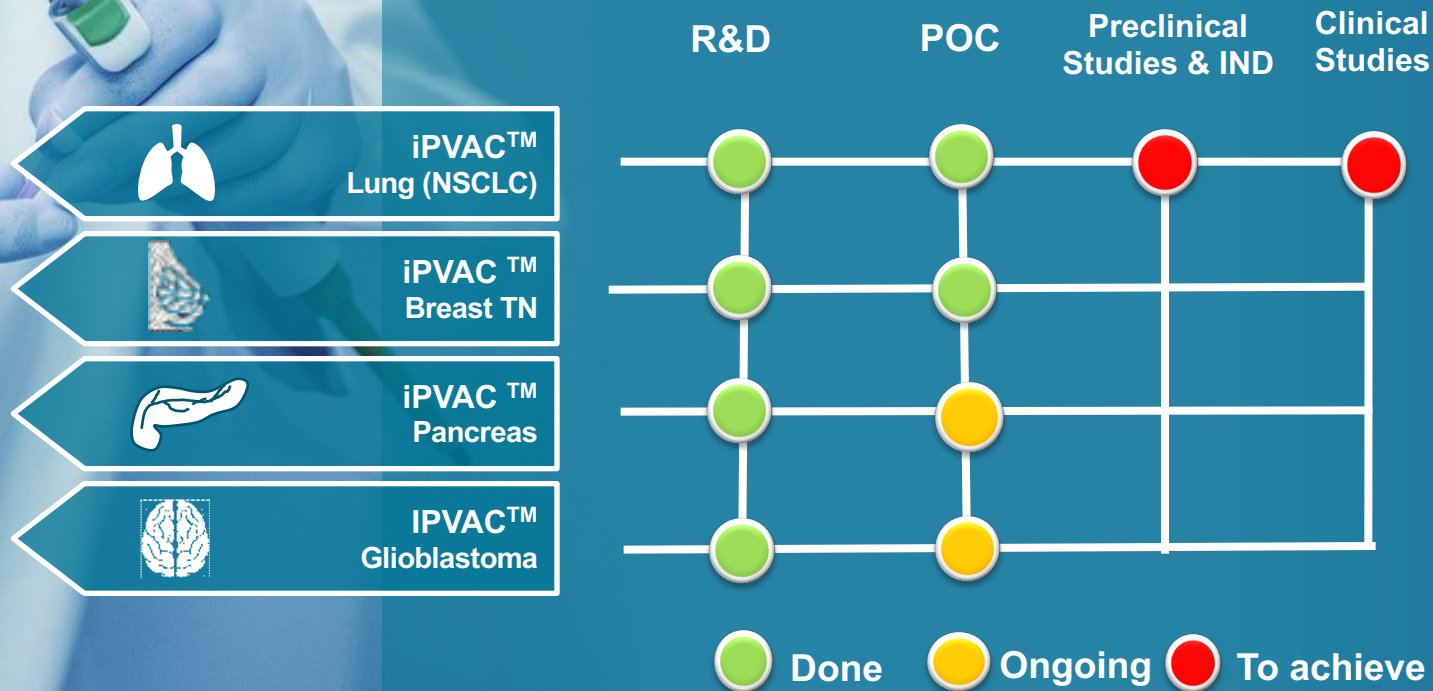
## 1st 'Pan-Cancer' Therapy



- Effective against all epithelial solid tumors with mesenchymal traits and 'embryonic stemness' phenotype (Oct4, Sox2, Nanog..)
- Identification of a common molecular signature
- Tissue-agnostic therapy

# ADVANCING A PIPELINE OF FIRST-IN-CLASS IPVAC™ PROGRAMS

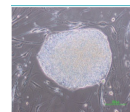
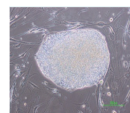
1st IPVAC (ESC) in several indications



# ADVANCING A PIPELINE OF FIRST-IN-CLASS IPVAC™ PROGRAMS

## 2<sup>nd</sup> Generation IPVACs (iPSC) for organ-specific cancers

**1st IPVAC  
EMBRYONIC  
STEM CELLS**



**2<sup>nd</sup> IPVAC  
INDUCED PLURIPOTENT  
STEM CELLS**

**Identical Properties**

- ❖ Self-renewal
- ❖ Illimited growth
- ❖ Differentiation to all cells

2012: Nobel Prize  
Shinya Yamanaka  
Kyoto University

**Blood cells**



**iPSCs**



**IPSIRIUS Platform:**  
Disruptive method of production of novel source  
of embryonic cancer neo-antigens.  
Precision medicine

# IPVAC™ PRODUCTS

## Competitive advantages

### Speed/Cost



- ❖ **Off-the-shelf** allogeneic cell therapy
- ❖ **Scalable & industrial** manufacturing process

### Access



- ❖ **Large number of patients**
- ❖ **Pipeline of multiple indications**
- ❖ Controlled cost

### Pipeline IO Programs



- ❖ **Multiple schedules and combination therapies**
- ❖ Repeat dosing
- ❖ Future randomized protocols  
Preventive / Curative
- ❖ Integrated capabilities from target discovery to clinical trials  
(Phase I/IIa, II/III)

# COMPETITION LANDSCAPE

## Start-up Developing PSC-based Immunotherapies



**PSC-based Immunotherapy (IPVAC )**

**ALLOGENEIC PSC (ESC & iPSC)**

**Industrialized approach**

**'Pan-cancer' & precision medicine approach**

**Anti-CSC curative & preventive therapy**

**France, Inserm**



**iPSC-based Cancer Vaccines**

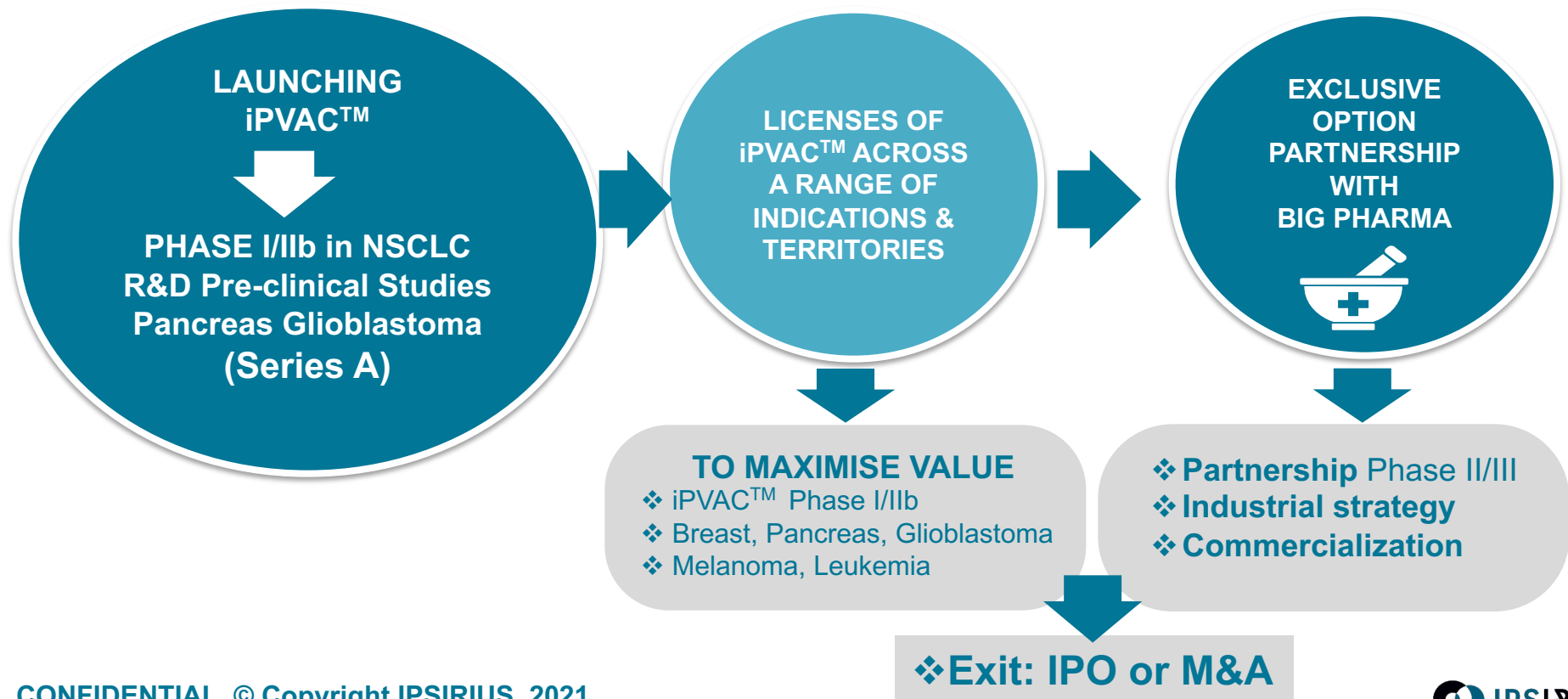
**AUTOLOGOUS iPSC**

**Personalized approach**

**Preventive therapy**

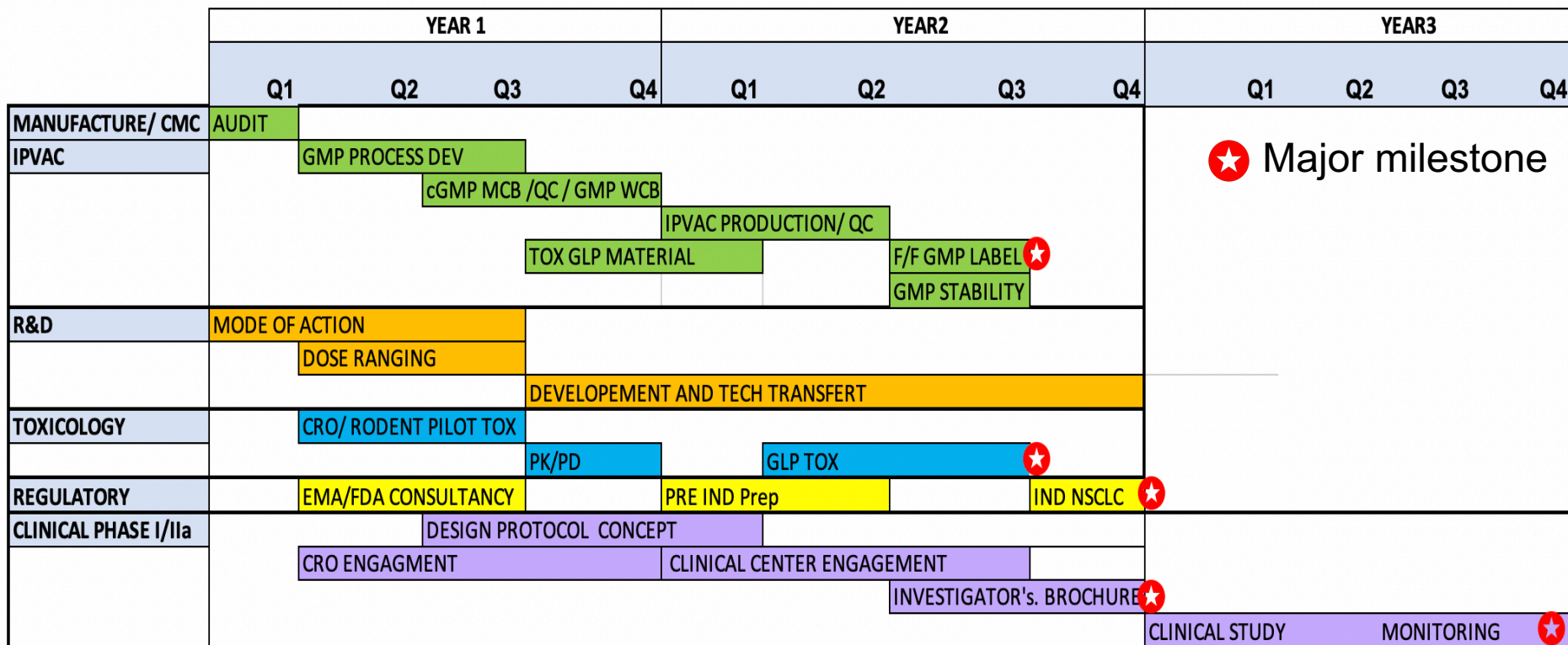
**USA, University of Stanford**

# BUSINESS MODEL



# DEVELOPMENT PLAN

## IPVAC™ IND On-Track in NSCLC for 1Q 2023



★ Major milestone



# FINANCING NEEDS

(€) Year 1-3

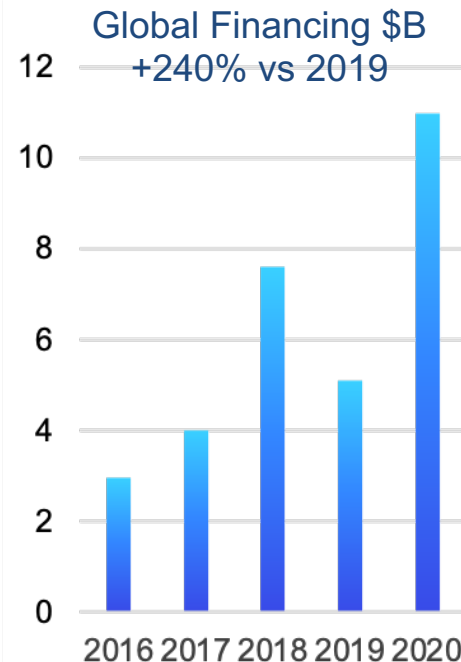
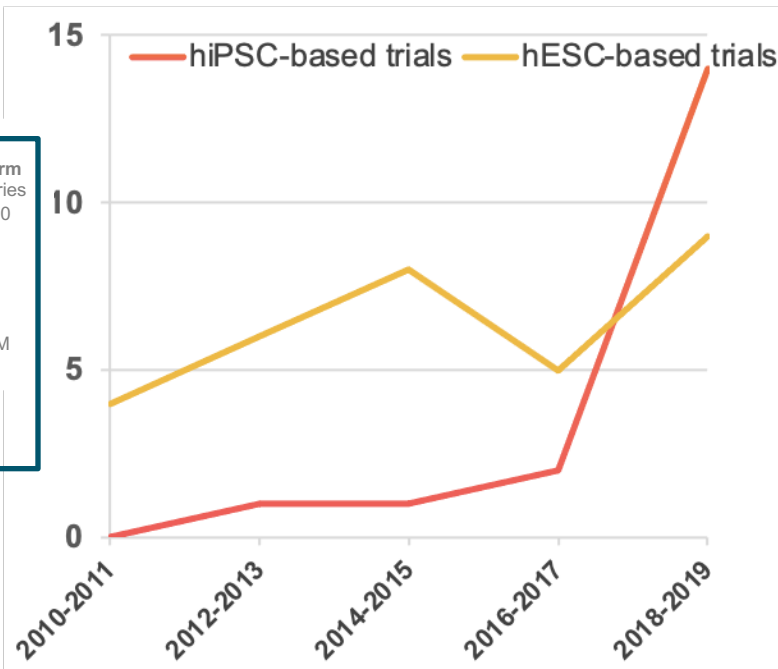
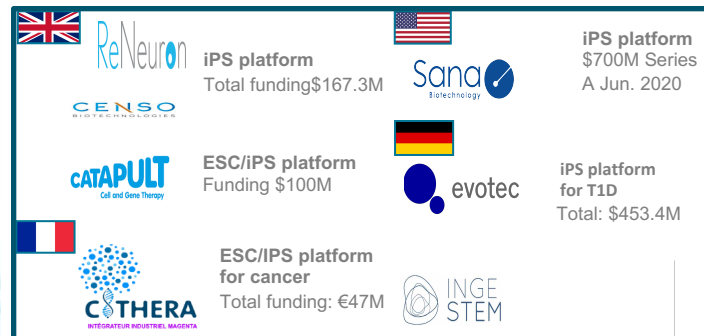
Cash Need - All Activities €'000s	Year 1	Year 2	Year 3	Total
Core Operation	1 068	1 068	992	3 128
Clinical Study	280	420	1 925	2 625
Manufacture & Toxicology & Regulatory	1 280	4 039		5 319
R&D	800	575		1 375
Patent	140	164	291	595
<b>Total</b>	<b>3 568</b>	<b>6 266</b>	<b>3 208</b>	<b>13 042</b>

- ❖ **Public non-dilutive grants** (European Grants, BPI, CIR) `
- ❖ Early clinical phase work **will boost upcoming Series B value** (manufacturing scale-up for 2<sup>nd</sup> phase I/IIa two IND programs)

# MARKET OF PSC

## A growing pipeline of allogeneic cell therapies based on iPS & ES

### ESC/iPS Platform



# COMPARABLE EARLY-STAGE DEALS IN iPSC-BASED THERAPIES

19



**2019** - Bayer acquires BlueRock Therapeutics (iPSC) platform  
\$240 m upfront + \$360 m milestones

**Deals value BlueRock up to \$1 billion** (40.8 % held by Bayer)  
Initial focus in neurology, cardiology, and immunology  
1st clinical program in Parkinson's



**2019** - Century Therapeutics, a Versant Ventures-created company  
\$250 m in financing commitments from Bayer, Versant and  
Fujifilm Cellular Dynamics Inc. (FCDI).

# WRAP-UP

## THE PROJECT IN A NUTSHELL (PART 1/2)



### OUR MISSION

Becoming a game changer in the immuno-oncology arena.  
Developing a disruptive universal cellular immunotherapy to treat advanced cancer.



### FOUNDERS

Pioneers in cell and gene therapies with 25 years of management experience in clinical and experimental oncology.



### INNOVATION STRATEGY

Building the future of oncology by targeting Cancer Stem Cells (CSC) at the root of cancers to eradicate once and for all the tumor.



### THE MARKET

Projection for 2025 : Leading pre-clinical assets IPVAC<sup>™</sup> for multiple refractory tumors: Lung, Breast ,Pancreas, Glioblastoma

# WRAP-UP

## THE PROJECT IN A NUTSHELL (PART 2/2)



### OUR COMPETITIVE ADVANTAGE

Pan-cancer cellular therapy targeting cancer stem cell compartment  
Off-the-shelf scalable allogeneic cell therapy medicinal products



### FINANCING REQUIREMENTS

€13 million (Series A + non-dilutive grants)



### USE OF FUNDS

Generating the first in class stem-cell based immunotherapy IPVAC™ in lung cancer.  
Pipeline development of other indications



# Thank you

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*Join us to Win and Cure  
Cancer Forever*