# A Global Leader

## in Oncolytic Immunotherapeutics

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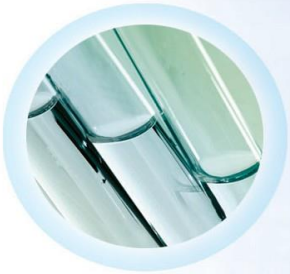

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# Company Overview

## SILLAJEN, INC. (215600:KS)

- Chairman and CEO: Dr. Eun Sang MOON, MD
- Founded in 2006 as a research collaborator to Jennerex, Inc.
- March 2014 acquisition of Jennerex
- $140m IPO onto KOSDAQ in December 2016

### Seoul

- Corporate management
- Finance/accounting/legal
- R&D Planning

### San Francisco

- Medical affairs
- Clinical operations / Regulatory Affairs
- Preclinical & translational science
- Technical operations (CMC & Quality)
- Business development

### Busan & Yangsan Research Lab

- Discovery
- Nonclinical/translational research
- Supporting assay work

# Corporate Identity

## Biotechnology Company Developing Immuno-Oncolytic Virus

### Innovation

- Developing first-in-class, immuno-oncolytic virus (IOV) based on vaccinia virus
- Distinctive genetic engineering technology to modify virus
- Efficacious cancer treatment through unique, multiple mechanisms

### Excellence

- Experts from global Big Pharma with extensive clinical experiences
- Global clinical network through partnerships
- Technology built upon strong patent portfolio
- **Orphan Drug designation**: Marketing Exclusivity
- Differentiated know-how on manufacturing processes

### Growth

- Significant unmet needs in the liver cancer market
- Expandability to other solid tumor types such as kidney cancer and colon cancer
- Used in combination to enhance existing blockbuster drugs: Big Pharma is racing to find their combination partners
- Developing next generation IOVs based on SOLVE® platform

**Targeting, Attacking and Eradicating Cancers**

A Global Leader in Oncolytic Immunotherapeutics

# Expect Event Rich 2019

## Pexa-Vec

- Completion of patient enrollment in China for Phase III for 1L HCC (PHOCUS)
- BLA preparation and commercialization partnerships in anticipation of PHOCUS readout & completion
- Potential data from REN026, Phase Ib trial for 2L RCC in combination with LIBTAYO® (Cemiplimab)
- Potential data from NCI Phase 1/2 trial for mCRC in combination with IMFINZI® and Tremelimumab
- Potential data from multiple partner-sponsored combination trials (Combination with OPDIVO®, YERVOY®, etc.)

## JX-970

- Ongoing preclinical studies with academic collaborators and data publications
- IND preparation and potential initiation of Phase 1 basket trial for α-PD-1, α-PD-L1 immunotherapy refractory patients

## Next Generation

- Ongoing in-house research and academic collaborations for next-generation candidate development

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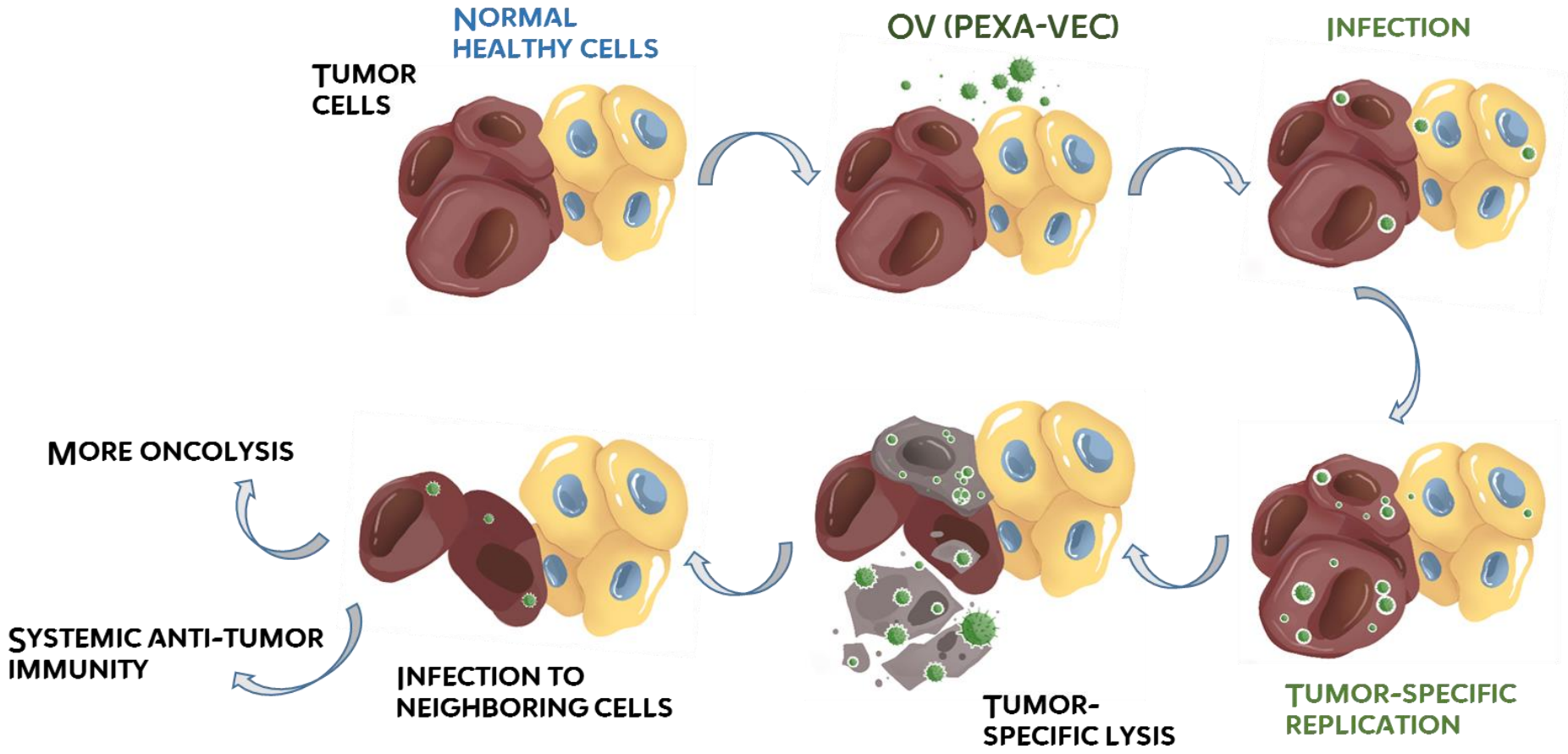
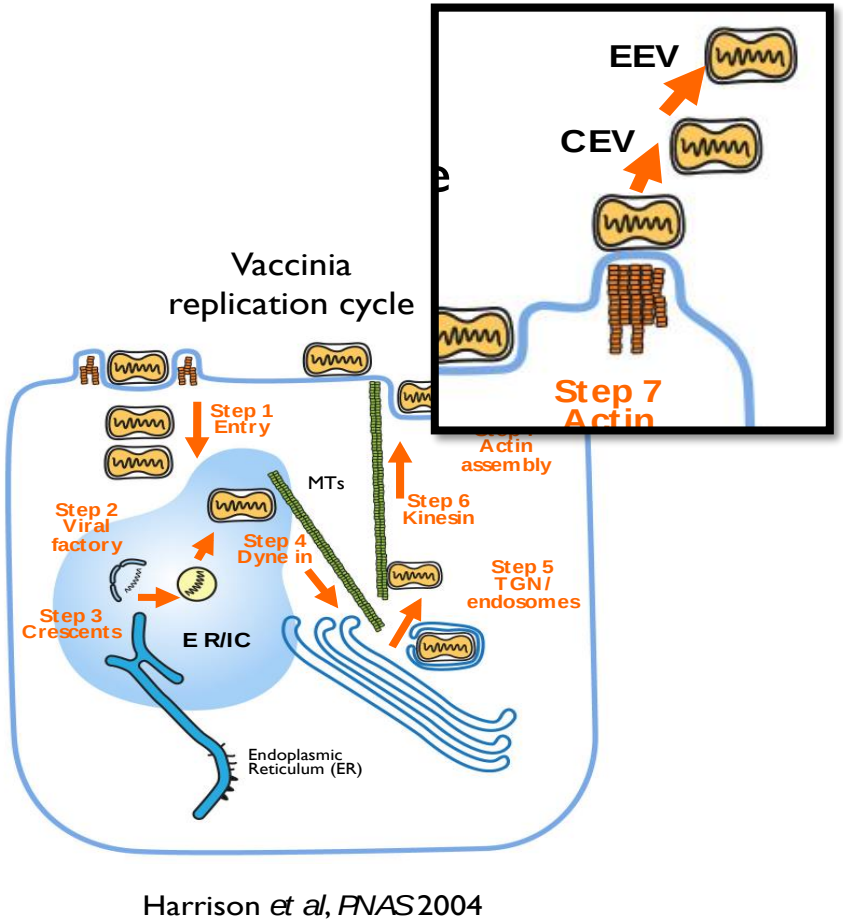
# THE SCIENCE

# Oncolytic Virus : Selectively Targets and Destroys Cancer Cells



# Why Vaccinia as Oncolytic Immunotherapy Platform?




Harrison *et al*, *PNAS* 2004

**Multiple advantages**

- Applicable for various tumor types
- Targets cancer cells and tumor vasculatures
- Large transgene arming capacity

**Intravenous**

- Evolved for systemic spread: stable in blood
- Unique stealth EEV evades complement & antibody mediated clearance

**Safety**

- Inoculated safely into millions of humans through smallpox vaccines
- Excellent, well-described safety profile

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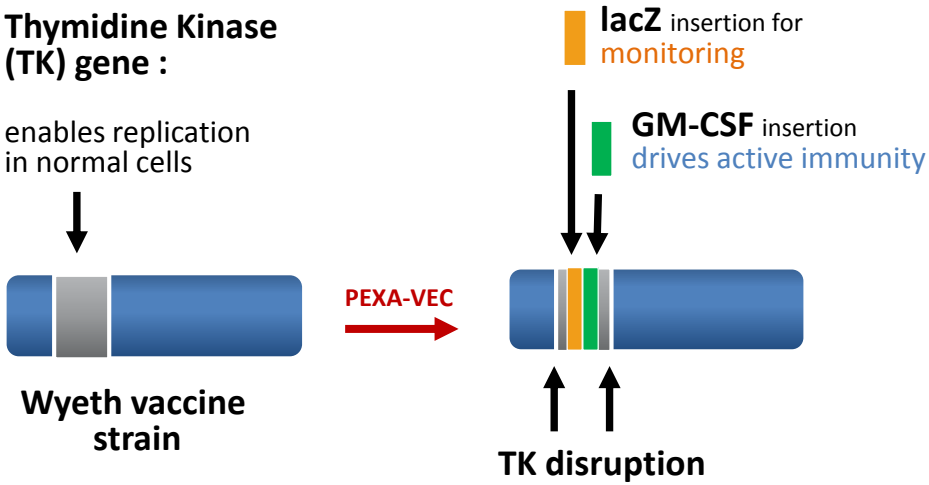
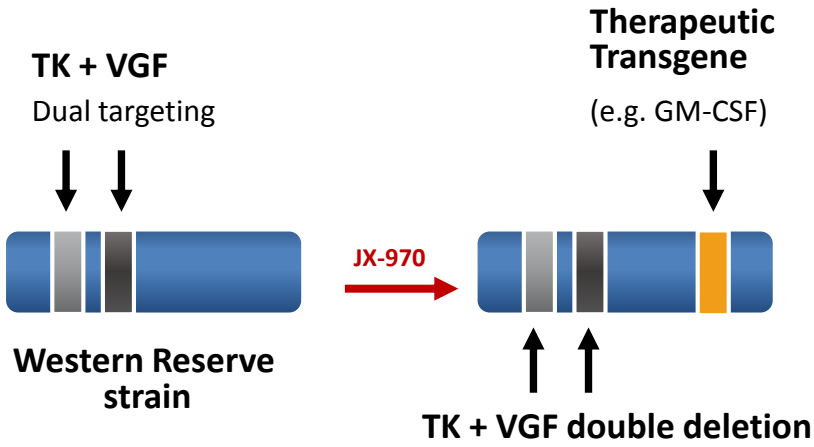
# SillaJen's Product Pipeline

## Pexa-Vec (JX-594)

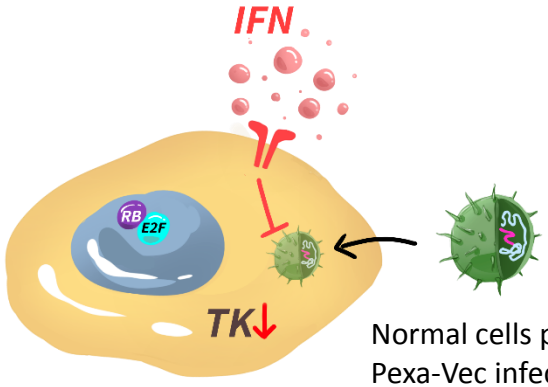



## JX-970

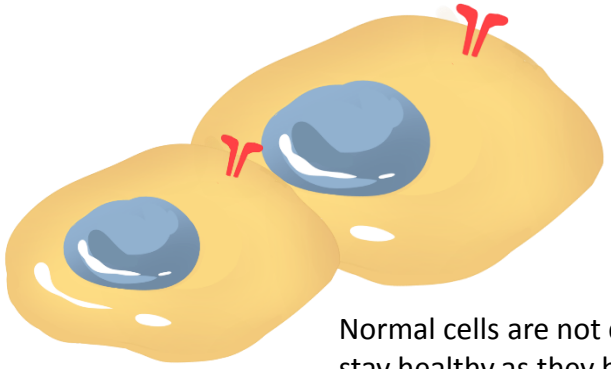



- Genetically modified vaccinia (Wyeth and Western Reserve strains)
- "Attenuation" via TK (thymidine kinase) gene inactivation: provides tumor selectivity & safety (VGF deletion in JX-900 for added safety)
- GM-CSF added to activate systemic immunity (dendritic cell maturation, T-cell stimulant) for Pexa-Vec and JX-970
- LacZ as a marker gene

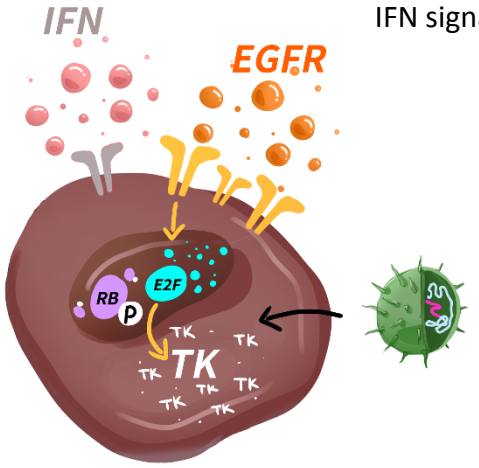
# Tumor Targeting: Engineering to Exploit Pathways Commonly Activated in Tumors



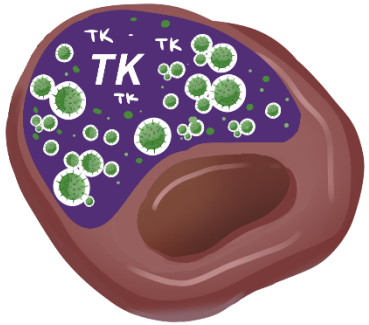

Normal cells provide innate defense against Pexa-Vec infection and replication via intact IFN signaling pathway and low TK activity



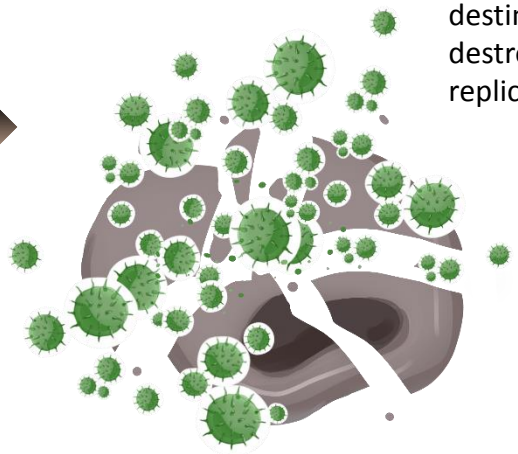
Normal cells are not damaged and stay healthy as they have the natural ability to clear Pexa-Vec




Frequent mutations in the IFN pathway and abnormally activated cell growth pathways (e.g. EGFR pathway) provides very high level of TK activity in tumor cells

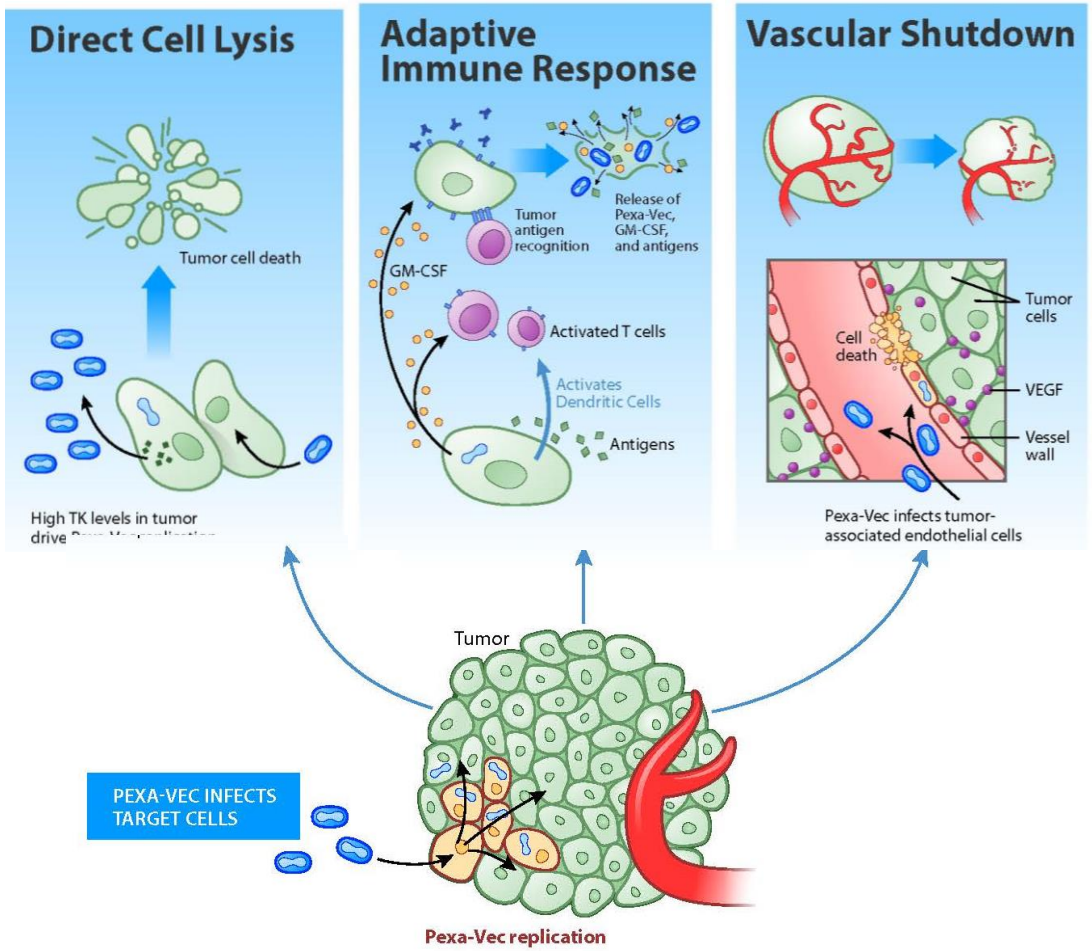



TK-deficient Pexa-Vec is able to replicate its progeny in the tumor cells by exploiting the constitutively active TK



Tumor cells are destined to be destroyed via vigorous replication of Pexa-Vec

# How It Works: Multiple & Complementary Anti-Tumor Effects




Kirn *et al*, *Nature Reviews Cancer* 2009

3-pronged attack on cancer: Direct lysis, immune activation, and antivascular activity by viral replication and spread:

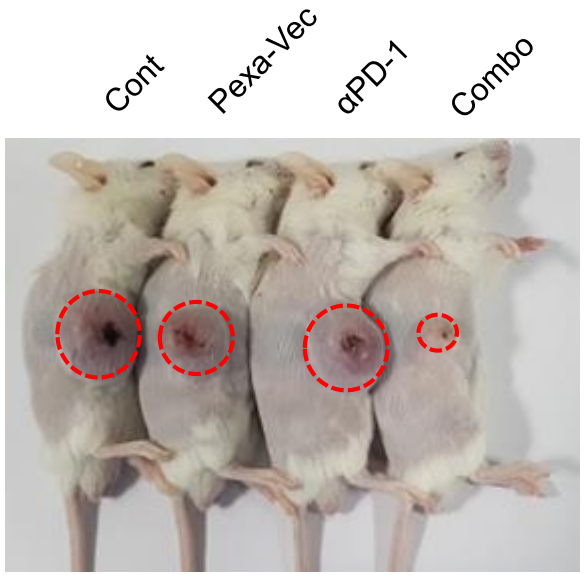
1) Tumor selective intratumoral replication of the virus leads to lysis of the infected cancer cell and spread to adjacent cancer cells

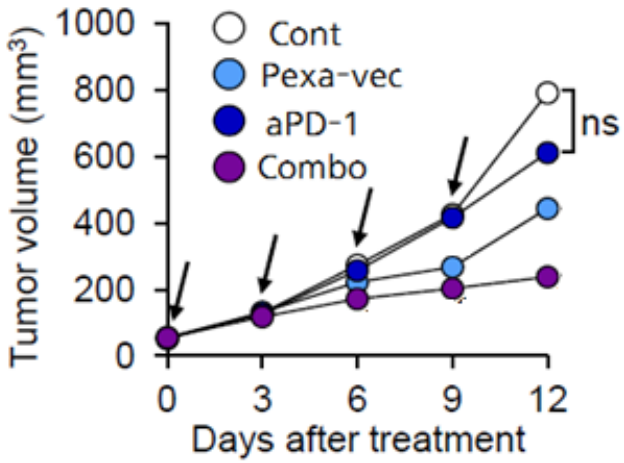
2) Induction of tumor-specific cytotoxic T-lymphocytes and "arming" for expression of therapeutic transgene products (e.g. GM-CSF) enhance immune response to the tumor

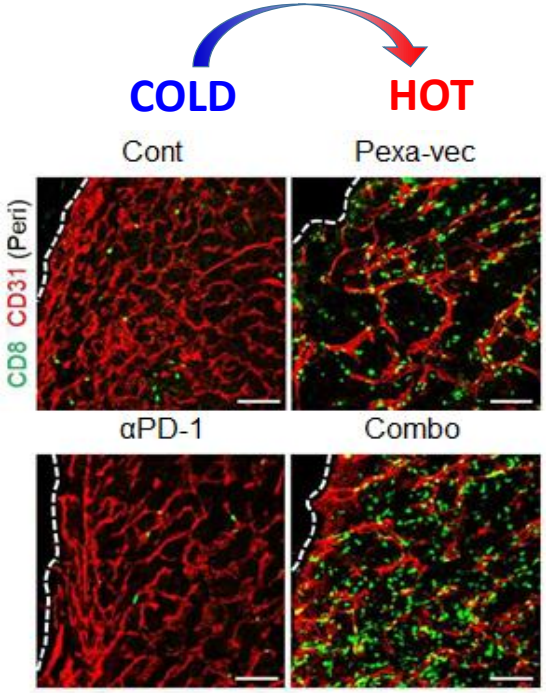
3) Blood flow to tumors can be blocked following intratumoral replication and spread

# Turning Cold into Hot: Combination with Immunomodulators Provides Opportunity to Increase Tumor Response

- Big Pharma is racing to find the most effective combination partners of immune checkpoint inhibitors (ICIs), which can turn cold tumor to hot tumor
- Cold tumors lack immune cells in tumor lesions, resulting in low response rates to ICIs. Converting cold tumors to hot tumors would result in the acquisition of responses towards ICIs
- Pexa-Vec 'heats' tumors, making them an easier and more attractive target for ICIs so they can be more effective at fighting cancer. Preclinical evidence strongly demonstrates the priming of immune system
- MASTERKEY-265: IMLYGIC®(T-Vec) + KEYTRUDA®(Pembrolizumab) combination clinical trial in melanoma
  ➔ The OV+ICI combination has garnered an increasing amount of attention in the Biopharma market



# CLINICAL DEVELOPMENT OVERVIEW:

Pipeline, Clinical Data, Key Studies

# Clinical Development Overview

- **Key clinical studies**
  - HCC (Liver Cancer): Ph 2 and 3 frontline
  - RCC (Kidney Cancer): Ph 1/2 treatment refractory
  - CRC (Colon Cancer): Ph 1/2 treatment refractory

- **>400 patients have received intratumoral and/or intravenous Pexa-Vec (>1,400 treatments)**
  - Enrolled across the globe from North America to Europe to Asia

- **Pexa-Vec treatment generally well-tolerated**
  - Transient flu-like symptoms
  - Transient hypotension

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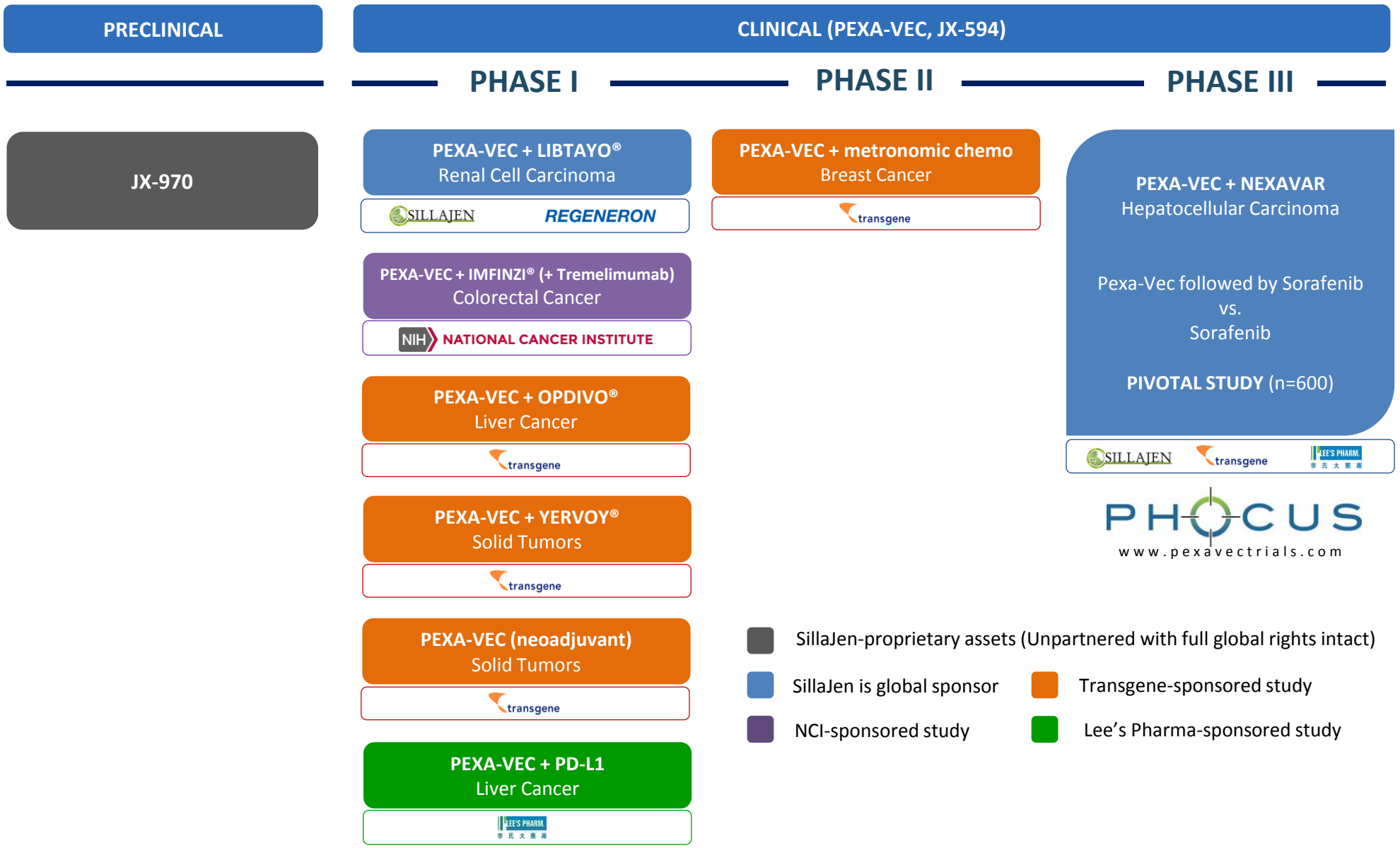
# Product Pipeline

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# Frontline HCC Phase III Study : PHOCUS

**PRECLINICAL**

JX-970

**CLINICAL (PEXA-VEC, JX-594)**

**PHASE I**

PEXA-VEC + LIBTAYO®
Renal Cell Carcinoma

PEXA-VEC + IMFINZI® (+ Tremelimumab)
Colorectal Cancer

PEXA-VEC + OPDIVO®
Liver Cancer

PEXA-VEC + YERVOY®
Solid Tumors

PEXA-VEC (neoadjuvant)
Solid Tumors

**PHASE II**

PEXA-VEC + metronomic chemo
Breast Cancer

**PHASE III**

**PEXA-VEC + NEXAVAR**
**Hepatocellular Carcinoma**

**Pexa-Vec followed by Sorafenib**
**vs.**
**Sorafenib**

PHOCUS
www.pexavectrials.com

**N = 600**

- Advanced-stage primary HCC
- Child-Pugh Class A
- No prior systemic therapy
(i.e. sorafenib-naïve, frontline)

- **Primary Endpoint:** Overall Survival (OS)
- **Key Secondary Endpoints:** Response by mRECIST, TTP, PFS, DCR

1:1 RAND

Arm A

Arm B

**Pexastimogene devacirepvec (PEXA-VEC)**

- 3 x IT q2wk
- 1 x $10^9$ pfu (plaque-forming units) per treatment

PEXA-VEC intratumoral → Sorafenib

Wk 0 — Wk 6

Sorafenib

**Sorafenib (NEXAVAR®)**

- 400 mg BID
- Until patient is no longer clinical benefiting or unacceptable toxicity occurs & at least until progression

Survival & Follow-up

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# LIBTAYO® (Cemiplimab) Combination

**PRECLINICAL**

JX-970

**CLINICAL (PEXA-VEC, JX-594)**

**PHASE I**

**PEXA-VEC + LIBTAYO®**
**Renal Cell Carcinoma**

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Colorectal Cancer

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Liver Cancer

PEXA-VEC + YERVOY®
Solid Tumors

PEXA-VEC (neoadjuvant)
Solid Tumors

**PHASE II**

PEXA-VEC + metronomic chemo
Breast Cancer

**PHASE III**

**PEXA-VEC + NEXAVAR**
Hepatocellular Carcinoma

Pexa-Vec followed by Sorafenib
vs.
Sorafenib

REGENERON

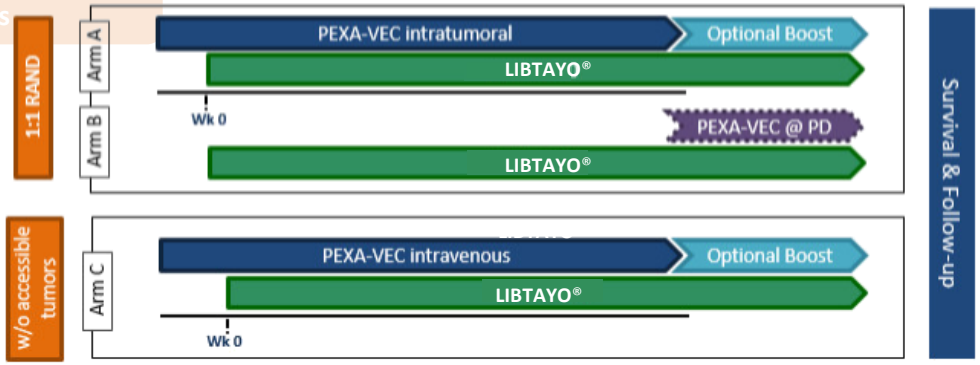
**N = 86**

- Metastatic RCC / Clear-cell variant
- Immune checkpoint inhibitor therapy naïve patients
- Tumor accessible for biopsy and injection (Arms A and B)

- **Primary Endpoint:** Safety
- **Key Secondary Endpoints:** ORR, PFS, OS, immune correlates

**Pexastimogene devacirepvec (PEXA-VEC)**

- IT starting D-X
- 1 x $10^9$ pfu (plaque-forming units) per treatment
- Optional boost starting Wk 27




**LIBTAYO®**

- IV q3wk
- Until progression (concurrent with PEXA-VEC following PD on Arm B)

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# IMFINZI® & Tremelimumab Combination

**PRECLINICAL**

JX-970

**CLINICAL (PEXA-VEC, JX-594)**

**PHASE I**

PEXA-VEC + LIBTAYO®
Renal Cell Carcinoma

**PEXA-VEC + IMFINZI® (+ Tremelimumab)**
Colorectal Cancer

PEXA-VEC + OPDIVO®
Liver Cancer

PEXA-VEC + YERVOY®
Solid Tumors

PEXA-VEC (neoadjuvant)
Solid Tumors

**PHASE II**

PEXA-VEC + metronomic chemo
Breast Cancer

**PHASE III**

**PEXA-VEC + NEXAVAR**
Hepatocellular Carcinoma

Pexa-Vec followed by Sorafenib
vs.
Sorafenib

NIH NATIONAL CANCER INSTITUTE

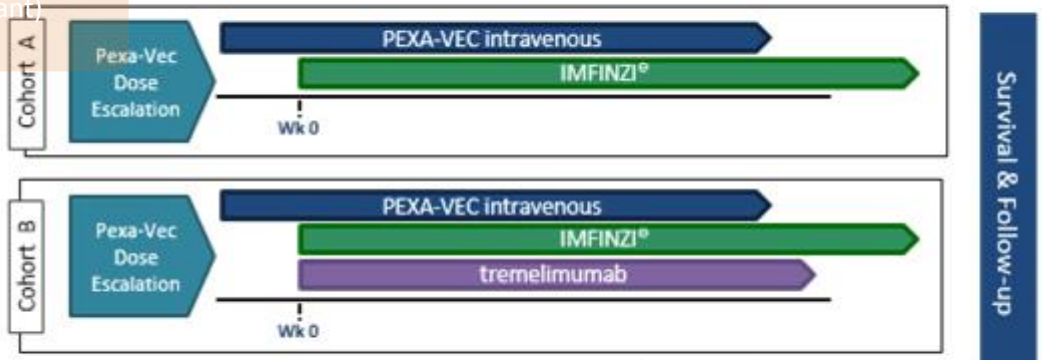
**N = 35**

- Metastatic CRC
- Microsatellite-stable (MSS or MSI-L) phenotype and $\alpha$-PD-1 therapy refractory MSI-H patients
- ECOG 0-1

- **Primary Endpoint:** Safety
- **Key Secondary Endpoints:** ORR, PFS, OS, immune correlates

**Pexastimogene devacirepvec (PEXA-VEC)**

- IV starting D-X




**IMFINZI® (durvalumab)**

- IV
- Until progression

**tremelimumab**

- IV
- Until progression

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# Single IV pre-operative administration of Pexa-Vec (NEOADJUVANT)

**PRECLINICAL**

JX-970

**CLINICAL (PEXA-VEC, JX-594)**

**PHASE I**

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**PEXA-VEC (neoadjuvant)**
**Solid Tumors**

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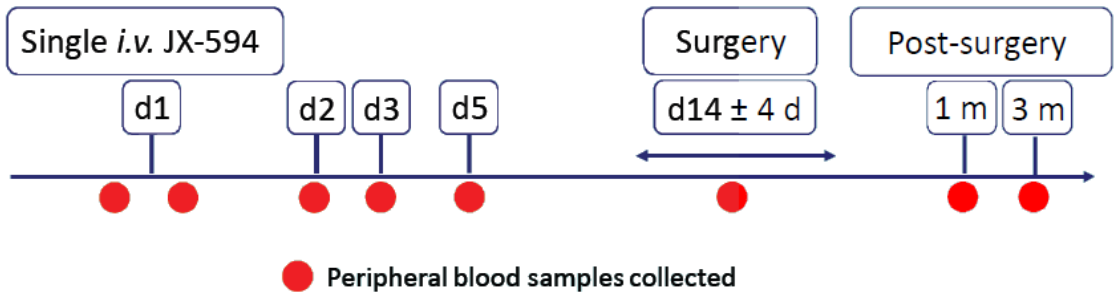


- Investigating the immunostimulatory effect of Pexa-Vec in patients with either colorectal cancer liver metastases (CRLM) or metastatic melanoma
- A **single dose** of $1x10^9$ pfu of Pexa-Vec administered by IV infusion to 9 patients (3 with metastatic melanoma, 6 with CRLM) prior to planned surgical resection

*ASCO 2018 Abstract #3092*

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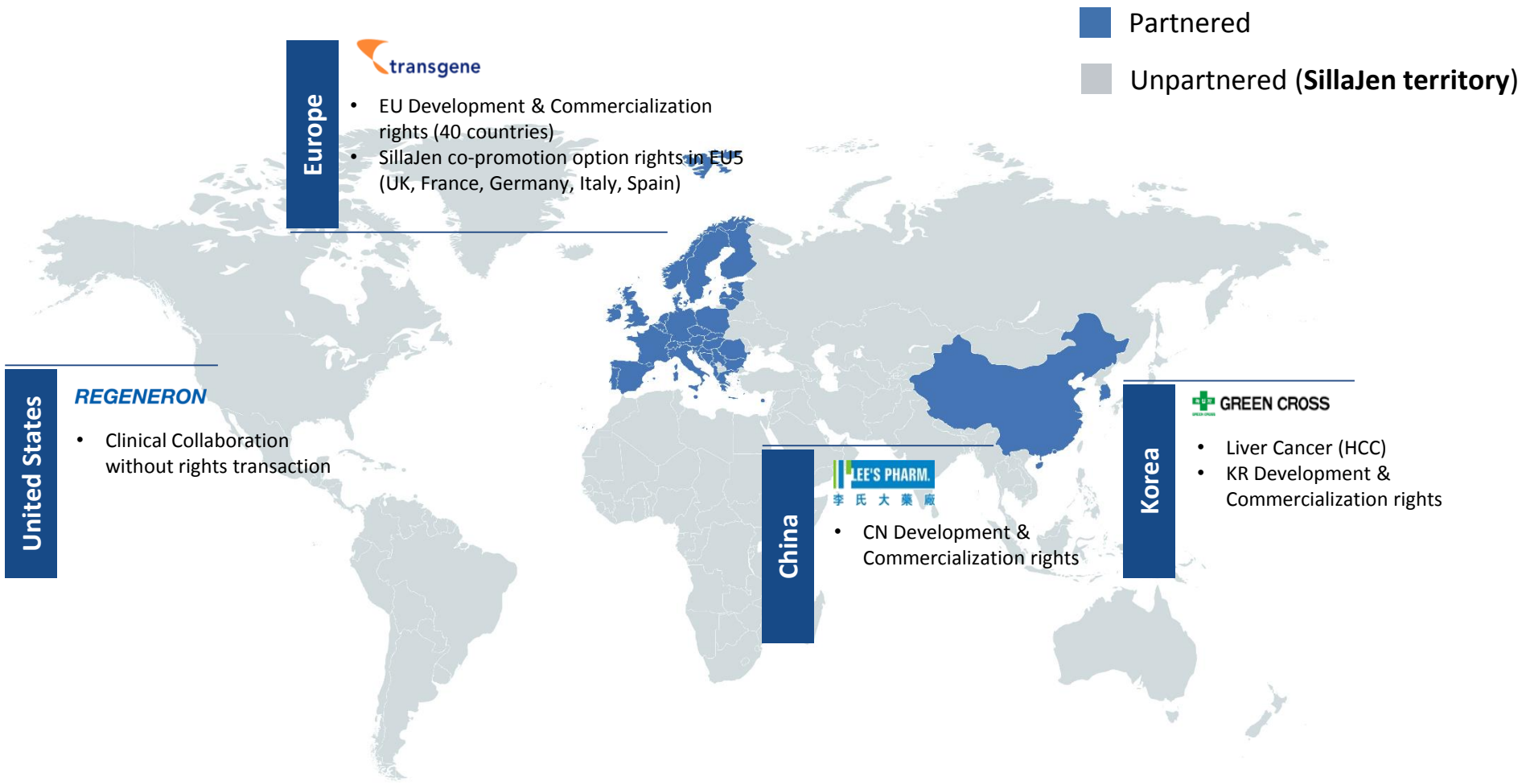
# PARTNERSHIPS AND DEVELOPMENT STRATEGIES

# Partnership




- All other assets (incl. JX-970) are unpartnered


www.sillajen.com