KOMABIOTECH biotechnology

SIRION BIOTECH

Viral Vector Technologies Enabling Gene & Cell Therapies

안녕하세요

Dr. CRISTINA I. URECHE

Any Gene to Any Cell

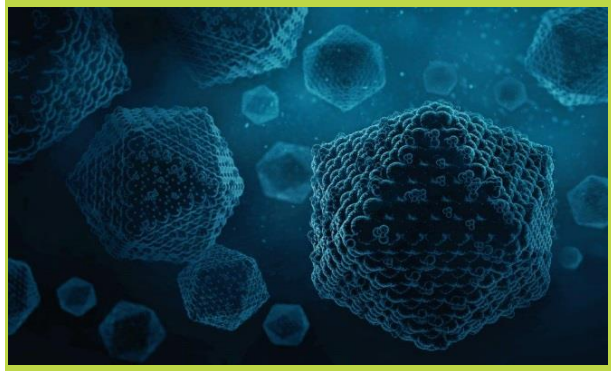
SIRION Biotech – ANY Gene to ANY Cell

Proprietary viral vector platform & complementary compounds for discovery & therapeutic applications

- Founded 2005, located in Martinsried/ Munich, Germany
- Constantly growing with 46% p.a. (2007-2018)
- Serving the entire value chain: discovery through preclinic to GMP
- Technology in clinical trials I/II/III
- First achievement of clinical milestone in 2016
- Offices & agents in the US, Japan, Korea, France, UK and Israel
- >200 industrial & academic repeat clients
- Global collaboration network with pharma, biotech & academia

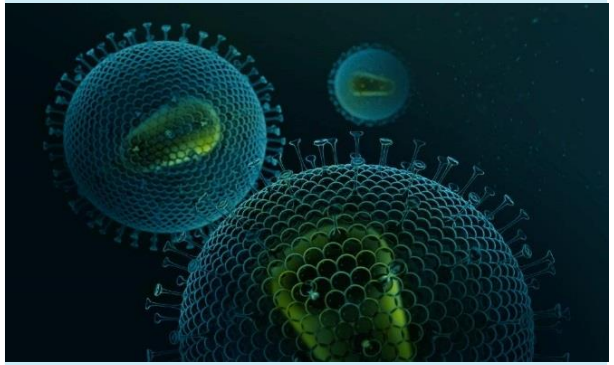
Our Unique Offer

AAV



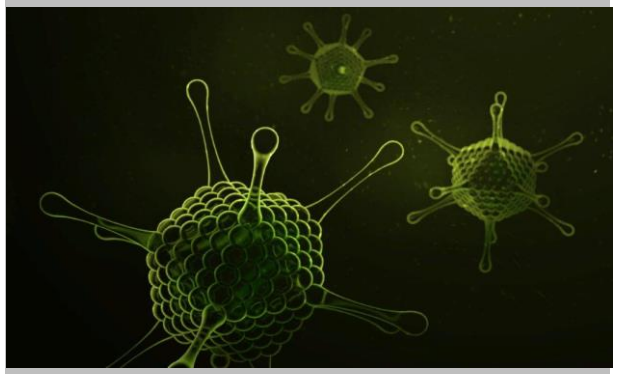
- Directed evolution
- Clinical vector design
- Vector engineering
- Non-GMP & GMP manufacturing

Lentivirus



- Transduction: LentiBOOST™*
- Clinical vector design
- Vector engineering
- Non-GMP manufacturing

Adenovirus



- Vaccination
- Proprietary BAC technology
- Vector engineering
- Non-GMP manufacturing

Multiple Applications

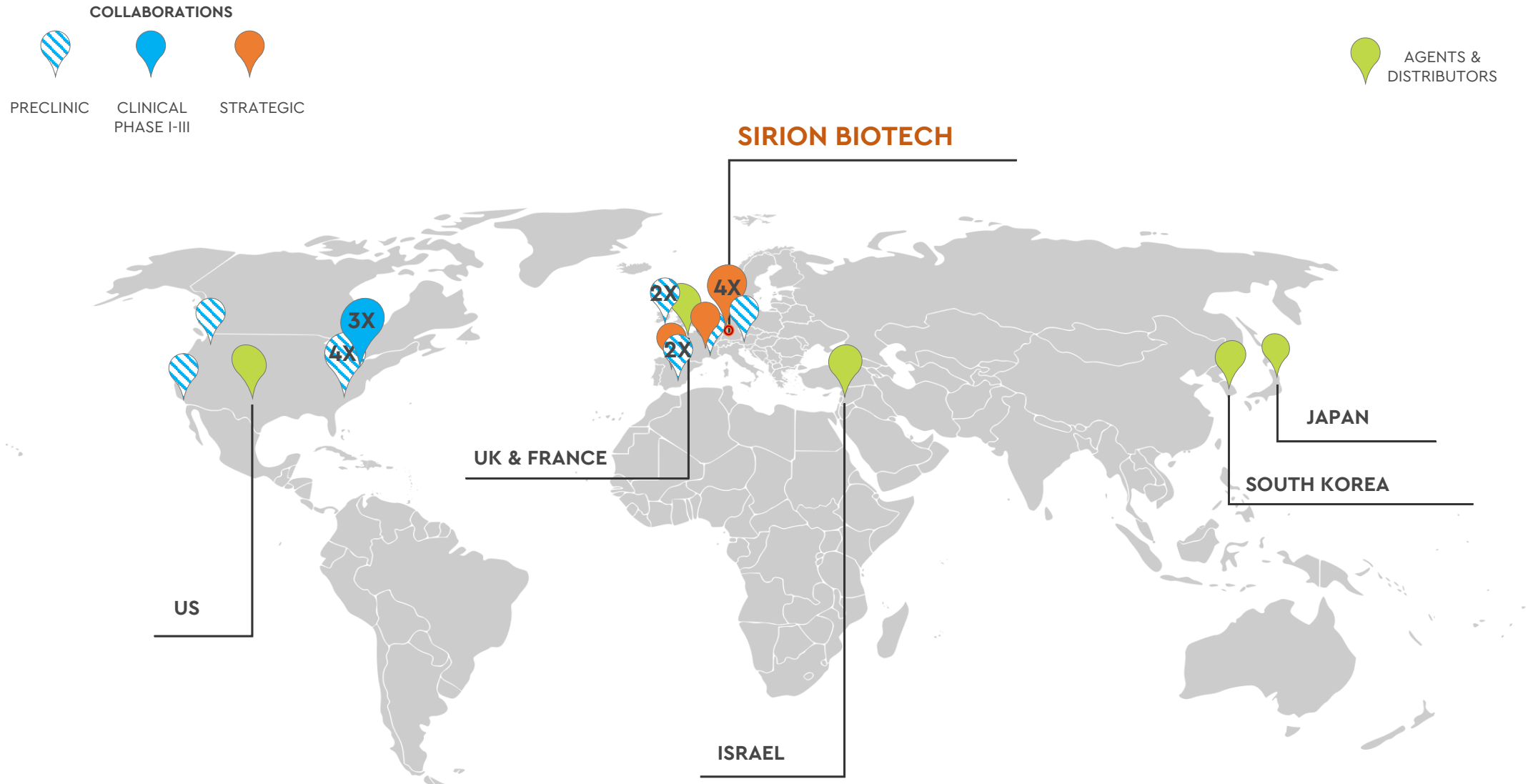
Drug discovery

Drug development

Gene/cell therapy

**** Transduction enhancer in cell therapeutic clinical trials I/II and III***

Global Presence & Collaboration Network



AAV VECTORS FOR GENE THERAPY

Project Management, Vector Optimization & Manufacturing

SIRION`s Gateway to Fast Clinical Vectors: Serving the Entire AAV Value Chain

- All serotypes
- Pilot-batches
- Up to 1E15 VG
- GMP-ready | Non-GMP TOX-batches

- All serotypes
- GMP Tox-batches
- Phase II

SIRION BIOTECH		CMO PARTNER
R&D	PRE-CLINICAL	CLINICAL

Drug Discovery & Development

- Target selection
- Lead identification & optimization
- Pharmacological profiling & mechanism of action (PoC)

In vivo NHP Studies

- Animal pharmacology (biodistribution)
- Dosing and administration route
- Safety (IND-Enabling Toxicology Studies)

Phase I/II to Phase III

- cGMP Manufacturing
- Pharmacokinetics
- Tolerability
- Side effects in healthy volunteers

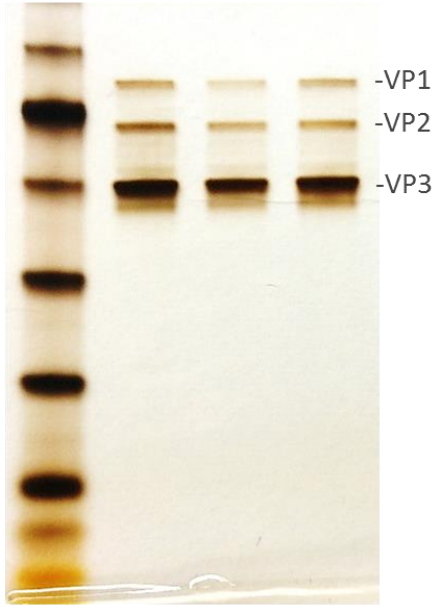
IND*

*Investigasional New Drug Submission

Our Unique Offer

- ✓Strong project & client commitment - Long term experience with industrial clients
- ✓Serving the **entire AAV value chain**: from **vector development** via **pre-clinic** to **GMP**
- ✓**Preclinic and GMP manufacturing with identical process and quality**
- ✓**Established manufacturing process** for all common AAV serotypes - no need for technology transfer/ process development (PD)
- ✓**Centralized communication**: Seamless process transfer from development to GMP partner
- ✓**Scale up** capabilities and **high end 2 step purification**

2-Step purified AAVx vectors

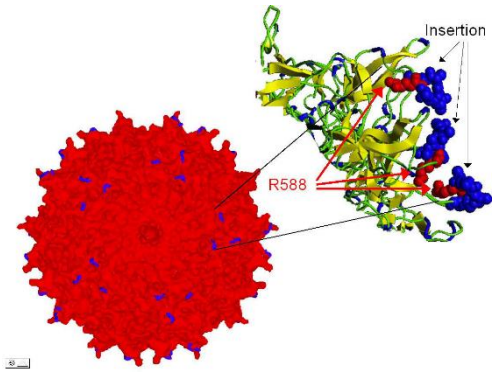


SDS gel Silver Stain

AAV Capsid Optimization Strategies

Peptide insertion libraries	Shuffled AAV libraries	Vector specificity	Immunologic optimization
Directed Evolution AAV ▪ Proprietary library designs ▪ Evolution for AAV1-12 available ▪ Capsid modeling to enhance cell specificity ▪ Selection in vitro and in vivo	**Next generation AAVs** ▪ Complex Shuffled AAV libraries ▪ Shuffling of AAV1-12 vectors ▪ Deconvolution software	**NGS-guided AAV evolution** ▪ NGS guided evolution of AAVs in vitro and in vivo ▪ Biodistribution of AAV variants ▪ Barcoded AAV libraries for complex biodistribution of multiple AAVs	**AAV immune evasion** ▪ Alanine scanning of VRs for all AAV serotypes ▪ nAB neutralization assay for capsid variants ▪ Combinatorial immune evasion library screening ▪ Preclinical testing of immune evasion variants

1. Müller et al., Nature Biotech. 2003
2. Waterkamp et al., J Gene Med. 2006
3. Ying et al., Gene Ther. 2010
4. Varadi et al., Gene Ther 2011

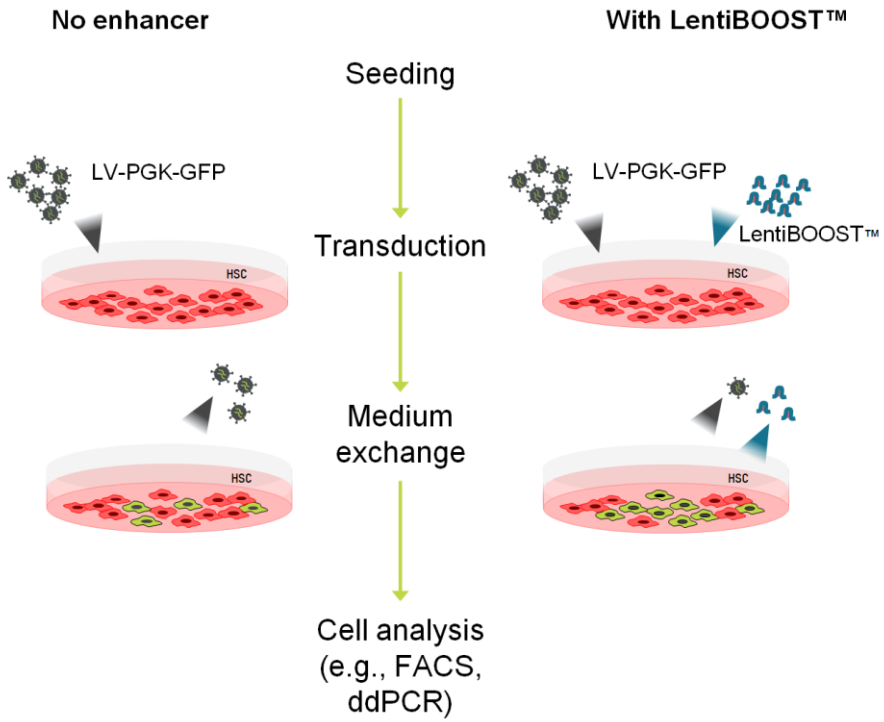


LentiBOOST™

- Transduction Enhancer -

LentiBOOST™: Mechanism of Action and Unique Features

- Is a amphiphilic poloxamer-based adjuvant
- Non-toxic and **universal adjuvant** (receptor independent)
- Facilitates fusion of lentiviral vectors with cell membrane without causing **cell depolarization and damage**
- **Acts in synergy** with all classes of transduction enhancers or spinoculation to maximize gene expression in a wide range of cells
- Available for preclinical and clinical developments **(GMP grade)**

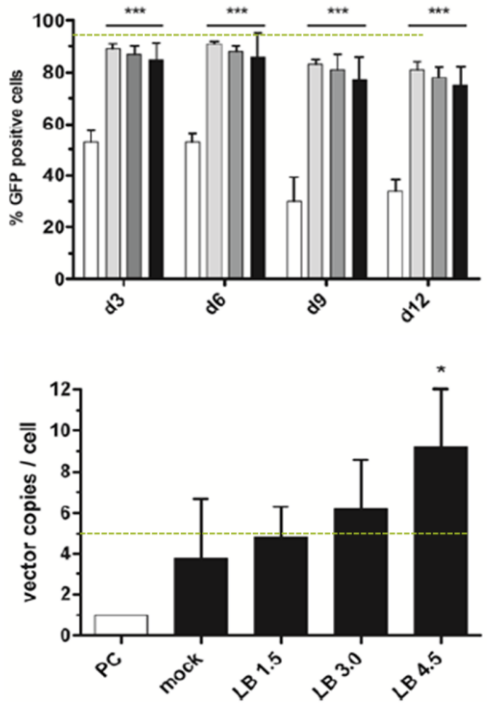


LentiBOOST™ can be easily integrated into any transduction protocol using Lentiviral vectors (e.g. CD34+ stem cells)

LentiBOOST™ Enables Efficient Transduction of Clinically Relevant Cells

CD34+ Stem Cells

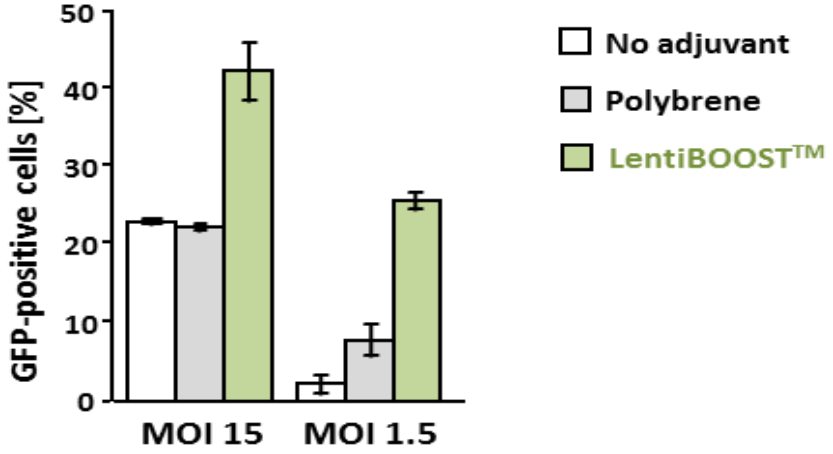
- >80% transduction efficiency
- High viability >86% for all conditions tested
- favorable conditions for cell growth – up to 30% increase
- Maintained stem cell character after transduction



LentiBOOST™ enhances lentiviral transduction efficiency in HSCs at low MOI, while maintaining low vector copy numbers per cell.

Primary T Cells

- Optimized transduction efficiencies at low MOIs
- Increased safety
- Reduced costs of good
- Up to 4x increase in cell number ⟹ for optimized manufacturing!



LentiBOOST™ elevates lentiviral infection of IL2/OKT3 stimulated PBMCs (peripheral blood mononuclear cells).

Clinical Benefits at a Glance

Clinical benefit demonstrated

- Clinical benefit shown in ongoing trials: US Ph III and PhI/II (e.g. *NCT03315078*) and Europe Ph I/II

Improved LV transduction efficiency up to 90%

- positive impact on success rate of clinical trials

Positive effect of cell proliferation

- reduced cost of goods, optimized LV manufacturing

Available in GMP grade, Drug Master File deposited

- regulatory benefits, facilitated IND filing

Low purchase price for the GMP substance

- reduced cost of clinical trials, reduced COGS

LentiBOOST™

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