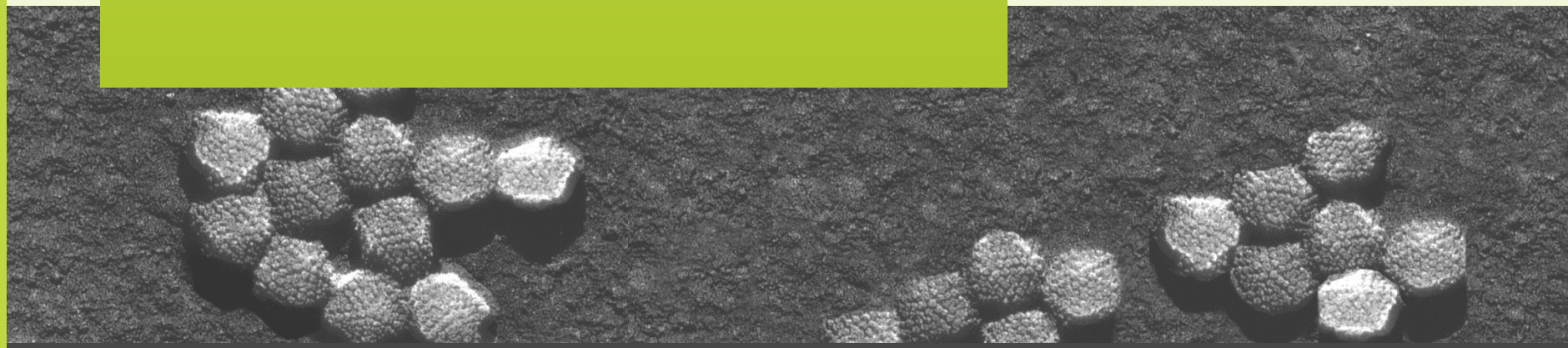
SIRION BIOTECH

Global Leader in Viral Vector Technologies

Gene Therapy – Vaccines - Discovery



SIRION BIOTECH – ANY GENE TO ANY CELL

Expert for viral vectors

- Competitive proprietary viral vector platforms
- High-end enabling technologies for AAV, LV, AV
- Strong focus on gene therapy and vaccines
- Technologies achieved Ph-I and Ph-III approval
- Founded 2005, 25 FTE in Munich
- Representations in US, Japan, Korea, France, Benelux, UK, Israel

Business – Fee for Service and Licensing

- Viral vectors for drug discovery and preclinical
- Development & licensing of proprietary enabling technologies, customized next generation viral vectors & breakthrough cancer vaccines

EFFICIENT & HIGHLY SPECIALIZED VIRAL VECTORS

SIRION BIOTECH

DRUG DISCOVERY

Custom made viral vectors

- unique vector designs
- highest quality standards
- fast turnaround time

Gene function analysis

- gene knockdown
- over-expression
- genome editing

In-vivo disease modeling

Cell based assays

GENE THERAPY

Next generation AAVs

- vector optimization
- capsid variant generation
- immunogenic profile improvement

Superior LV transduction

- LV BOOST reagents for substantially enhanced LV transduction
- LV antibody retargeting for higher specificity

IMMUNE ONCOLOGY

New class of cancer targets

- Gene-encoded tumor antigen
- Expression epigenetically regulated
- Immunosuppressive mode-of-action
- Preclinical validation in vivo

Adoptive T-cell therapies

- LentiBOOST for CAR-T/TCR manufacturing
- Targeted knock-in of TCR locus

VACCINATION

Ad19a/64

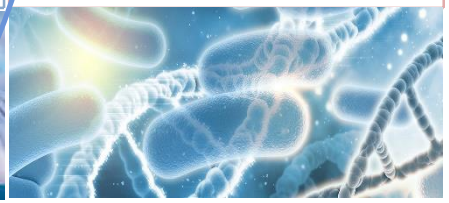
- highly immunogenic rare AV platform
- preclinical validation in NHP models for HPV

BAC technology

- proprietary platform for generation of rec. AVs

HCMV vector platform

- Single-cycle replication (in preclinical validation)



AAV – IN VIVO GENE THERAPY

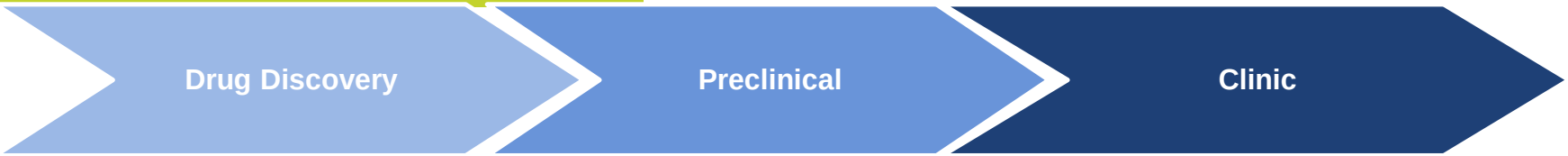
SIRION OFFERS COMPREHENSIVE AAV TECHNOLOGY

Service Business

- Long standing expertise in optimal vector design
- Tissue specific promoters & enhancers
- GMP compliant production protocols
- Unique purification protocols for highest purity / concentration
- Empty/full capsid ratio determination
- highest quality standards with batch to batch reproducibility
- fast turnaround time

Co-Development Projects

- Vector optimization
- Identify new **AAV variants** with **improved tropism**
  - Random peptide insertion
  - Shuffled libraries
- Generate new AAV variants with improved immunogenic response
- Highly selective AAV vectors with NGS-guided *in vivo* evolution

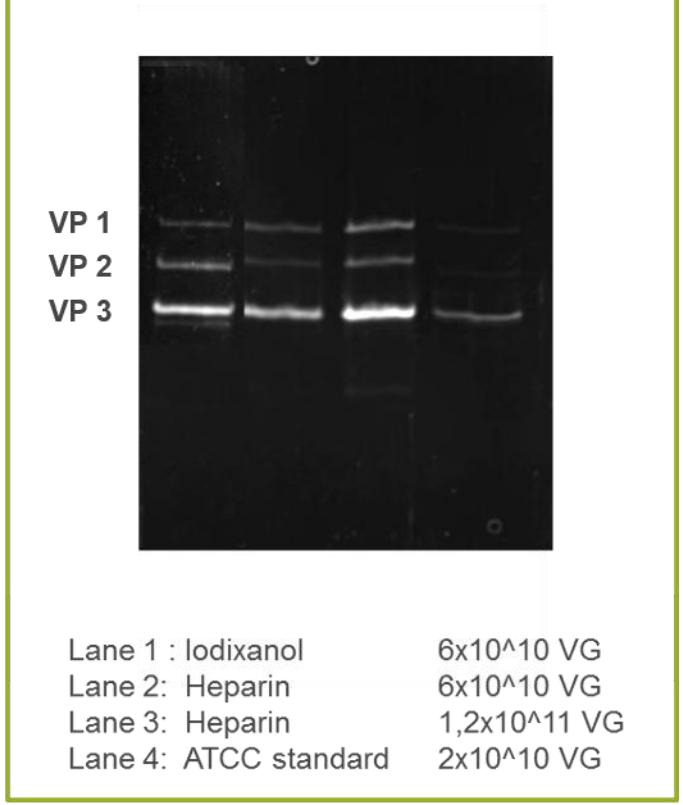


Fee for Service — **Collaboration & License Model**

AAV PRODUCTION SERVICES UNDER STRINGENT QUALITY CONTROL

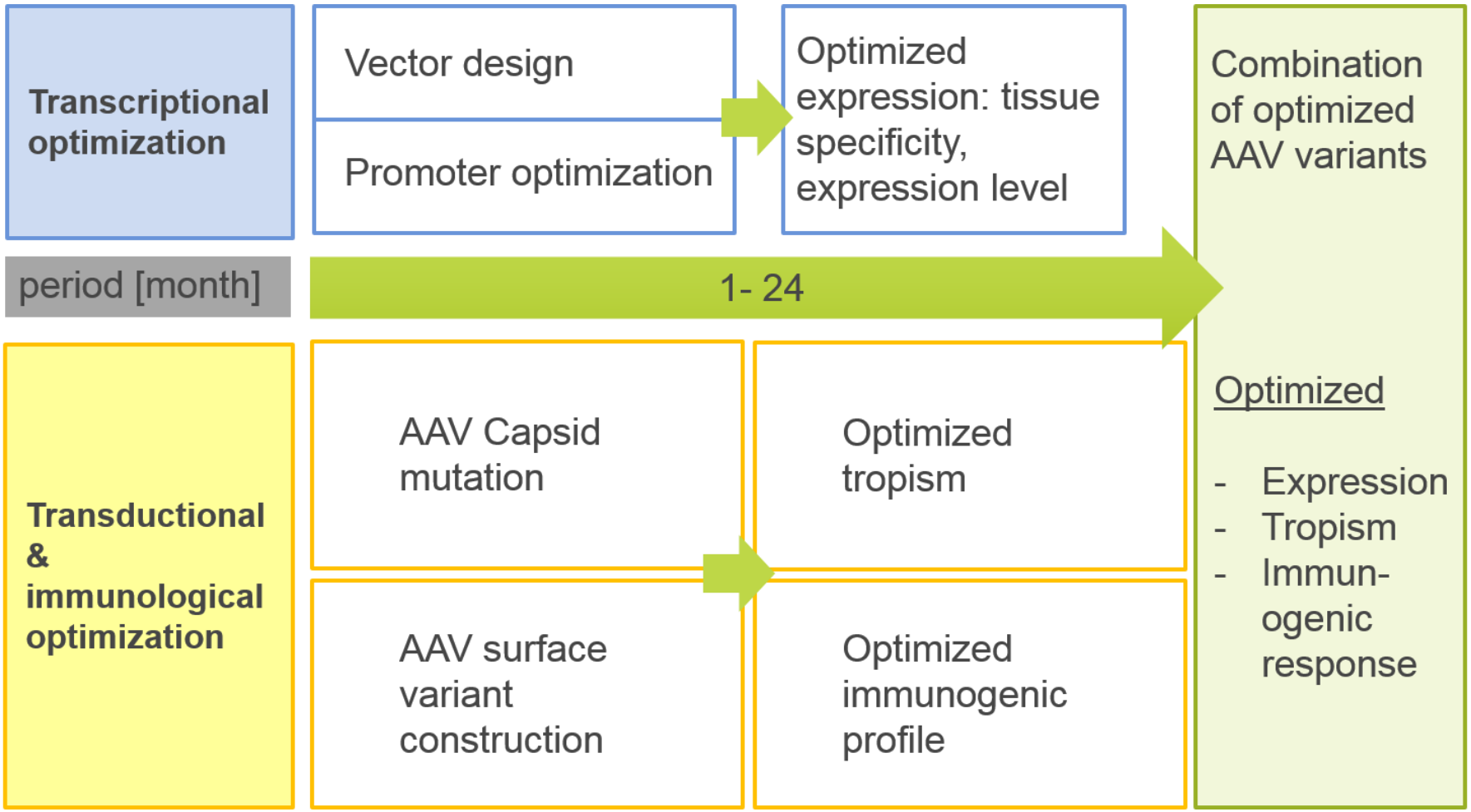
AAV Services	Standard
Total AAV particles delivered	- up to 5 x10^13 GC
Concentrated vector batches	- > 1 x10^13 GC/ml
Highly purified AAV particles	- Iodixanol gradient UC - Heparin affinity chromatography - ÄKTA
Production protocols	- GMP compliant*
Purity	- Analytic at protein level PAGE/ Silver staining - Separation of empty AAV particles*
Vector design	- Know-how/ advice on therapeutic designs - Fully customized
Functionality check	- In vitro test for batch to batch reproducibility
Quality controls	- Endotoxin/ sterility test

ssAAV6-CMV-targetX



* Available in 2018

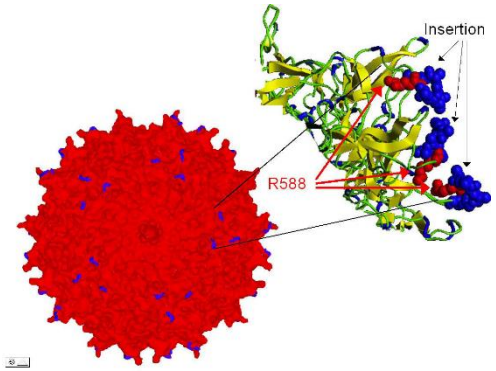
OPTIMIZATION OF AAV TISSUE SPECIFICITY & IMMUNOGENIC PROFILE – TRANSDUCTIONAL & TRANSCRIPTIONAL APPROACH



AAV CAPSID OPTIMIZATION STRATEGIES

Peptide insertion libraries	Shuffled AAV libraries	Immunologic optimization	Vector specificity
Directed Evolution AAV ▪ Proprietary library designs ▪ Capsid modeling ▪ Evolution for AAV1-12 available ▪ Selection in vitro and in vivo ▪ Academic collaboration network for preclinical expertise	**Next generation AAVs** ▪ Complex Shuffled AAV libraries ▪ Shuffling of AAV1-12 vectors ▪ Deconvolution software	**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	**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

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



LICENSING MODEL AAV

Research Agreement

R&D collaboration

- Standard Terms
- Development Costs
- Foreground IP

Commercial License Agreement

Milestone model including milestones and royalties:

- Development Milestones: Preclinical, Phase I/II, Phase III
- Regulatory & Commercial Milestones
- Net sales Royalties

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