Delivering differentiated genetic medicines to transform the lives of patients suffering from devastating diseases

LogicBio THERAPEUTICS

May 2021

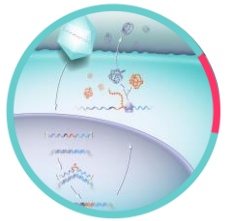
Forward-looking statements

This presentation contains "forward-looking statements" within the meaning of the federal securities laws. These forward-looking statements are not statements of historical facts and are based on management's beliefs and assumptions and on information currently available to management. Forward-looking statements include information concerning the Company's business strategy and the design, progression and timing of its preclinical trials and clinical trials, including information related to the Company's plans to initiate, advance and complete its planned SUNRISE Phase 1/2 clinical trial of LB-001 in methylmalonic acidemia ("MMA").

Forward-looking statements generally can be identified by terms such as "expects," "anticipates," "believes," "could," "seeks," "estimates," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would" or similar expressions and the negatives of those terms, and similar expressions and comparable terminology intended to identify forward-looking statements. The Company's operations involve risks and uncertainties, many of which are outside its control, and any one of which, or combination of which, could materially affect its results of operations and whether the forward-looking statements ultimately prove to be correct. Factors that may materially affect the Company's results of operations and whether these forward-looking statements prove to be correct include, among other things, that preclinical testing may not be predictive of the results or success of ongoing or later preclinical or clinical trials, that the development of the Company's product candidates and new platforms may take longer and/or cost more than planned and that the identification of new product candidates may take longer than planned, as well as those listed in the Company's Annual Report on Form 10-K filed on March 15, 2021 with the Securities and Exchange Commission ("SEC"), and the Company's subsequent Quarterly Reports on Form 10-Q and other filings with the SEC. In particular, the impact of the COVID-19 pandemic on the Company's ability to progress with its research, development, manufacturing and regulatory efforts, including the Company's plans to initiate, advance and complete its Phase 1/2 clinical trial for LB-001 in MMA, and the value of and market for the Company's common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the United States and in other countries, and the effectiveness of actions taken globally to contain and treat the disease. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

This presentation also contains estimates, projections and other information concerning the Company's industry, business and the market for its products and services, as well as data regarding market research, estimates and forecasts prepared by the Company's management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Certain data in this presentation was obtained from various external sources, and neither the Company nor its affiliates, advisers or representatives has verified such data with independent sources. Accordingly, neither the Company nor any of its affiliates, advisers or representatives makes any representations as to the accuracy or completeness of that data or to update such data after the date of this presentation. Such data involves risks and uncertainties and is subject to change based on various factors.

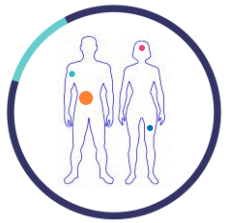
Clinical stage genetic medicine company aiming to deliver transformational therapies



GeneRide™ : a differentiated gene editing platform

sAAVy™ : a next generation AAV capsid platform

SUNRISE clinical trial for MMA, *in vivo* gene editing treatment for children



Potential to address a broad portfolio of genetic diseases early in patients' lives

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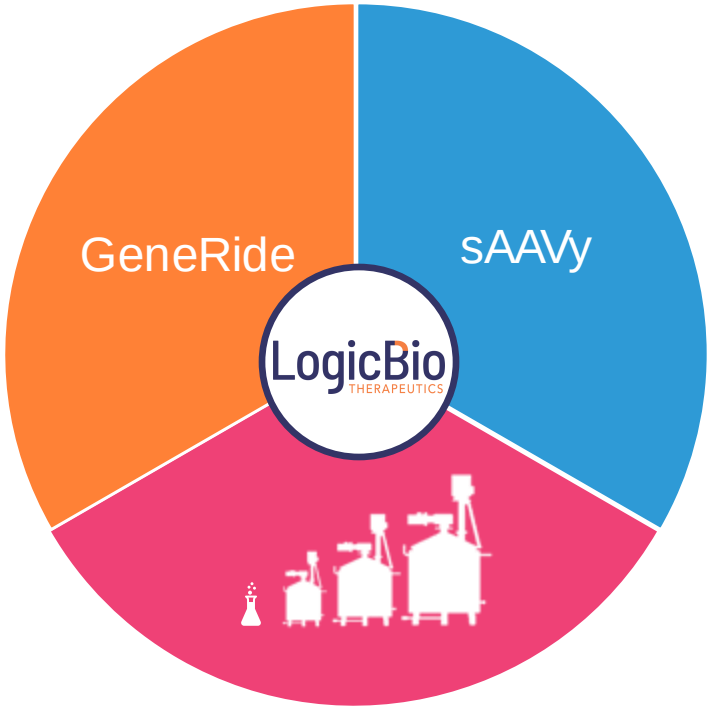
Pioneering a new class of genetic medicines

Combining innovative platforms to tackle a wide spectrum of diseases

GeneRide : a differentiated gene editing platform

- Nuclease free leveraging homologous recombination
- Durable therapeutic transgene expression driven by endogenous promoters
- Site-specific integration
- Modular and broadly applicable



sAAVy : a next generation AAV capsid platform

- Tissue tropism assessed in clinically predictive models
- High functional transduction
- Low immunogenicity
- High manufacturing yield

Process development and manufacturing

- Proprietary technologies
- Progressive internalization
- Focus on cost-effectiveness

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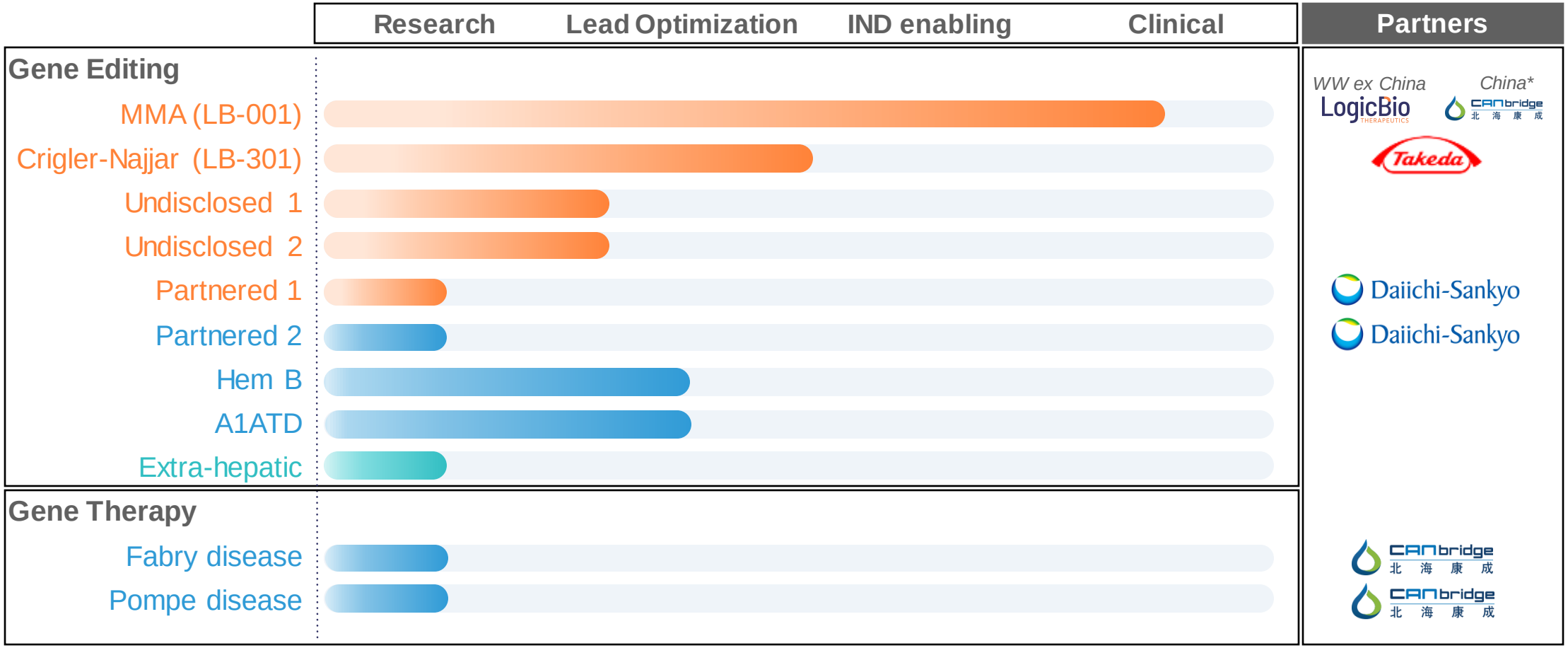
Pipeline leveraging GeneRide and sAAVy



*Option

Intracellular

Secreted

Expansion areas

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Expected 2021 Milestones

Initiating FIH clinical trial and building on our two innovative proprietary platforms

Clinical study	❑ Enroll first patient in SUNRISE trial ❑ Communicate operational updates for SUNRISE trial ❑ Present interim clinical safety and efficacy data
Pipeline	❑ Present translational data ❑ Declare at least one new development candidate ❑ Demonstrate enhanced transduction with sAAVy capsids
Platform	❑ Expand the platform to broaden therapeutic opportunities ❑ Report in-house high-yield manufacturing process ❑ Demonstrate efficiency of HR-driven integration at new loci

sunrise by LogicBio

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GeneRide Platform

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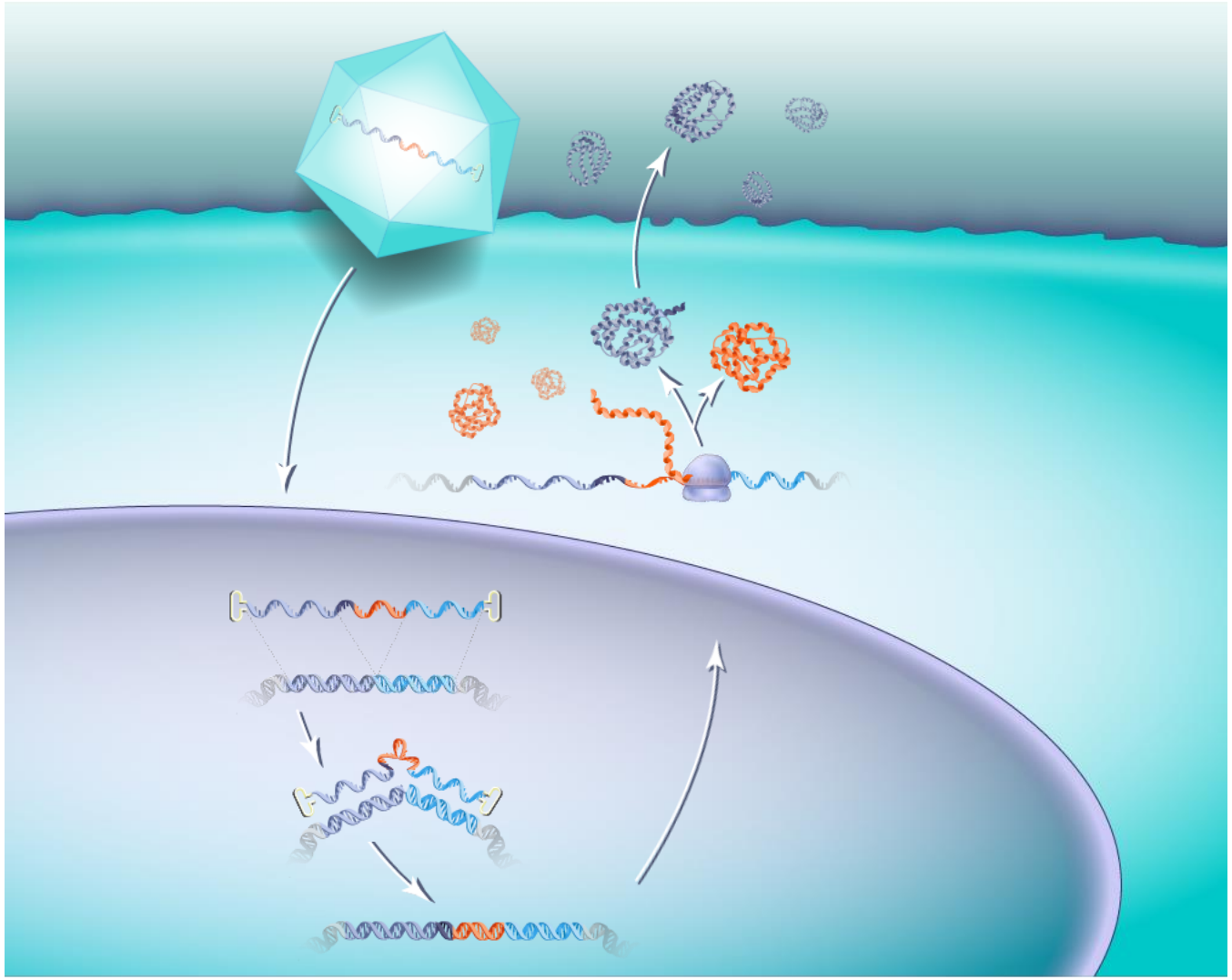
GeneRide: promoterless, nuclease-free gene editing platform



- Targeted cell entry
- Traffic to nucleus
- Site-specific recognition
- Homologous recombination driven integration
- Transcription of fused mRNA
- Polycistronic protein expression

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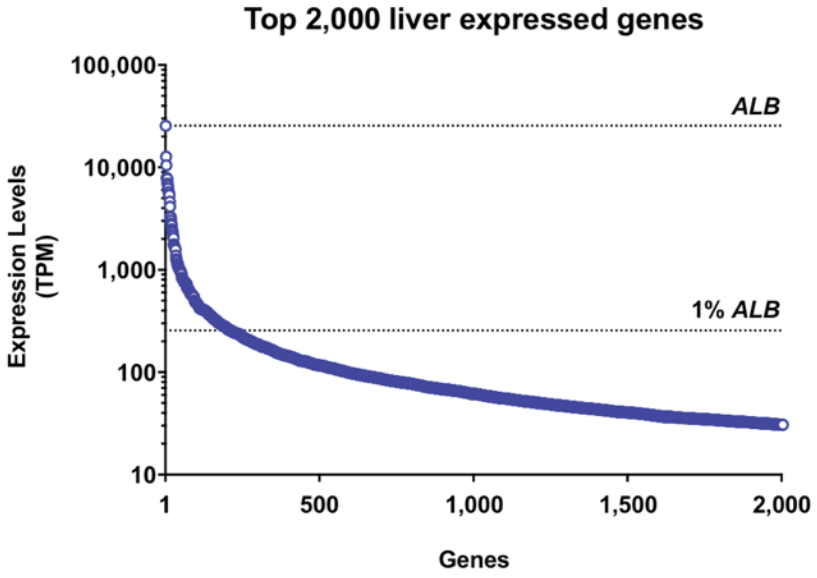
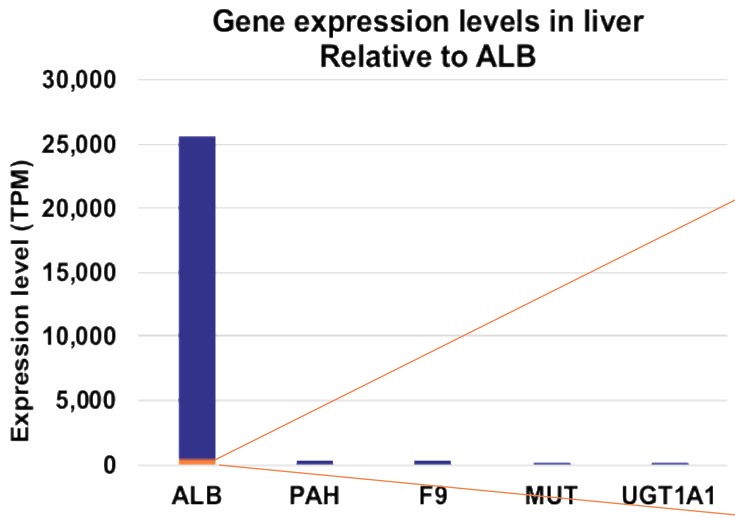
GeneRide enables therapeutic protein expression levels

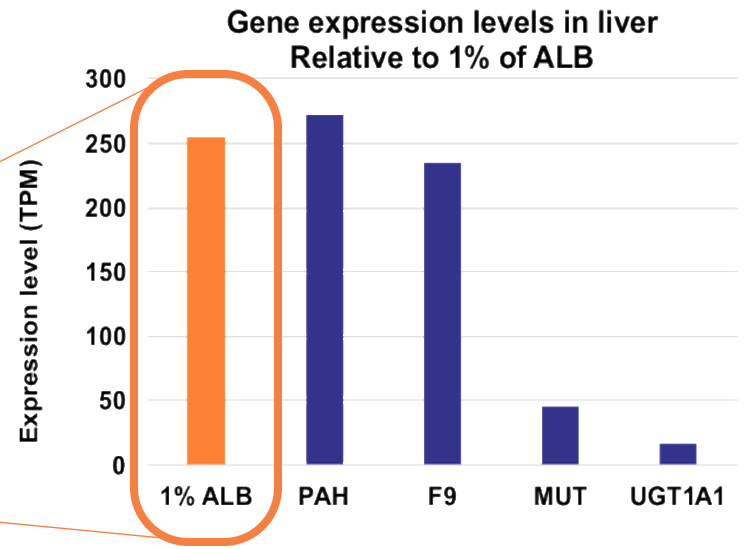
Taking a ride on albumin for liver-directed indications

Most abundant protein in circulation and the most highly expressed gene in the liver

Modest rates of integration at the *ALB* locus sufficient to achieve near-physiological expression levels of many disease-related liver proteins







Transcriptional profiling data from The GTEx Project

ALB – Albumin
PAH – phenylalanine hydroxylase (PKU)
F9 – Factor IX (Hemophilia B)

MUT – Methylmalonyl-CoA mutase (MMA)
UGT1A1 - UDP glucuronosyltransferase family 1 member A1 (Crigler-Najjar syndrome)

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GeneRide Platform
LB-001: Clinical Stage
Pediatric Patients with MMA

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Methylmalonic acidemia (MMA)

Life-threatening inborn error of metabolism with no pharmacologic treatment options

Epidemiology and Etiology:

- US Incidence: 1 in 50,000 births
- US Prevalence: 1,000 – 1,500
- On the newborn screening panel in every US state
- Organic acidemia caused by mutations in MMUT gene
- Results in the inability to metabolize certain amino acids and fats

Standard of Care and Outlook:

- Typically presents soon after birth
- Can be fatal in newborns, prognosis in survivors strongly influenced by early toxic events
- Restricted diet: strict low-protein, high-calorie
- Poor growth, developmental delay, frequent healthcare utilization
- No therapeutics, only aggressive management of symptoms
- Liver or liver-kidney transplants increasingly performed

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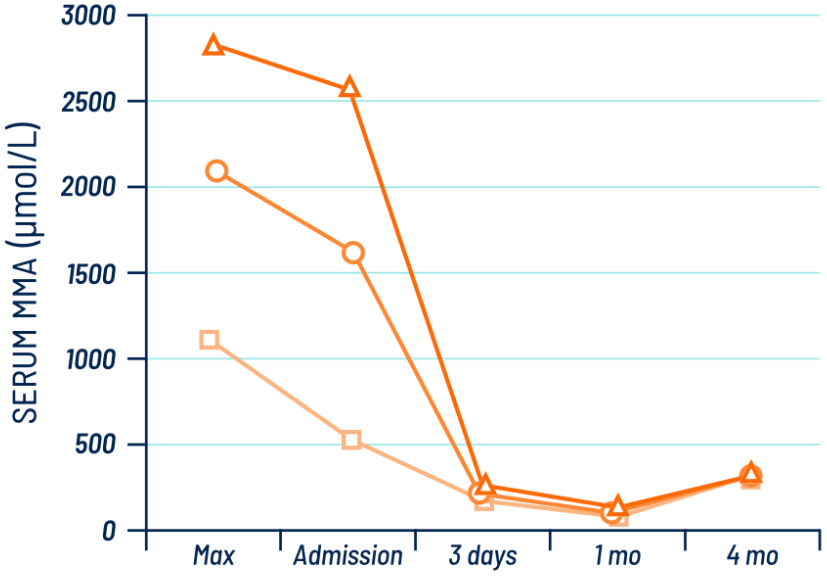
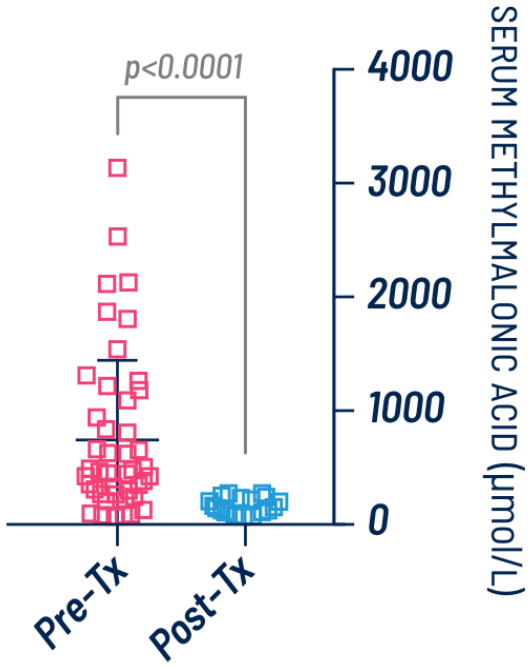
LB-001 goal: a "Molecular Liver Transplant"

Liver transplantation in young patients improves metabolic stability but may be accompanied by significant morbidity and is not readily accessible



[Niemi et al., J Pediatr, 2015]

LKT = Liver-kidney transplantation
LT = Liver transplantation



[Critelli et al., Liver Transpl, 2018]

- Finite number of liver donors
- Significant risks associated with surgery
- High procedural costs
  - *In U.S., approx. $880k and $1.3M for liver and liver-kidney transplantation, respectively*
- Lifetime dependence on Immunosuppressive drugs

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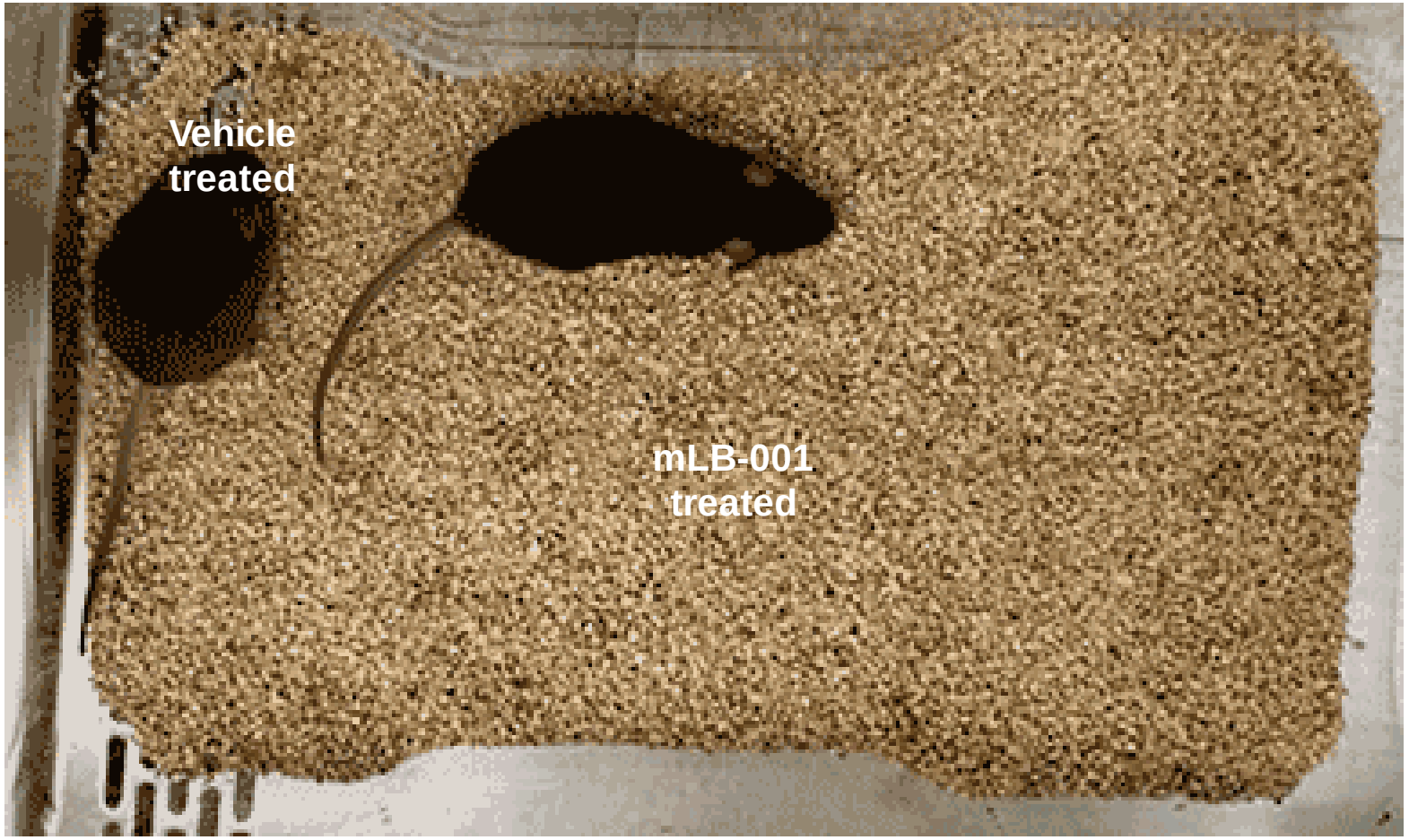
LB-001 protects MMA mice from metabolic crisis



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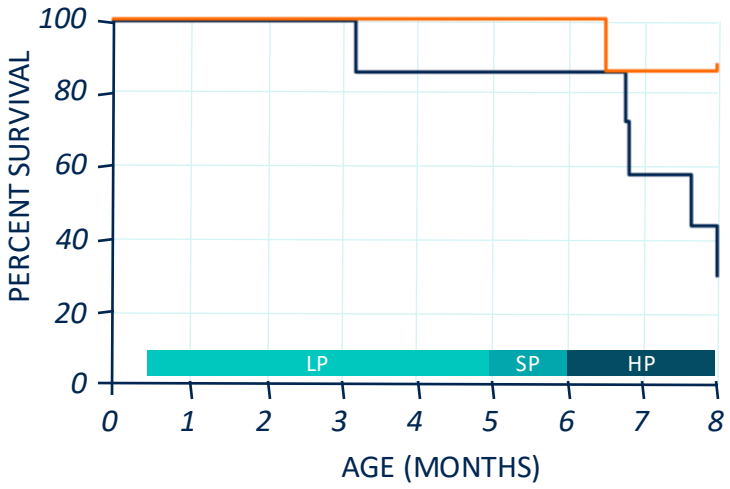
LB-001 protects MMA mice from metabolic crisis

Improves clinically relevant endpoints in a novel model of MMA

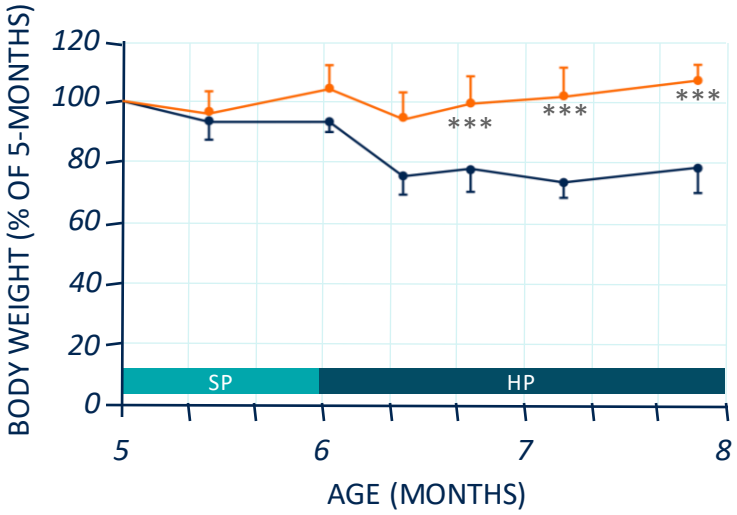
LB-001 improved survival



Treated (n = 7) Vehicle (n = 7)

p=0.052, log rank test

LB-001 improved growth

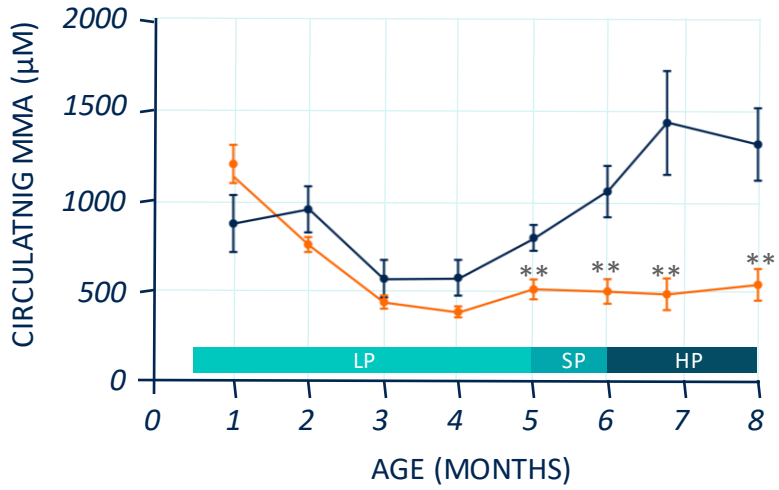


Treated (n = 7, 7, 7, 6, 6, 6)

Vehicle (n = 6, 6, 6, 6, 4, 4, 2)

***p=<0.001, Student's t-test, comparing groups at indicated time points

LB-001 prevented elevations in circulating MMA



Treated (n = 7, 7, 7, 7, 7, 7, 6, 6)

Vehicle (n = 7, 7, 7, 6, 6, 6, 4, 2)

**p=<0.01, Student's t-test, comparing vehicle and mLB-0.001 at indicated timepoints

Protein challenge to mimic metabolic crisis

LP LOW PROTEIN CHOW FOR DIET MANAGEMENT

SP STANDARD PROTEIN CHOW

HP HIGH PROTEIN CHOW

Adult mice dosed at 5×10^{13} vg/kg

Ko et al., *ASGCT*, 2020.

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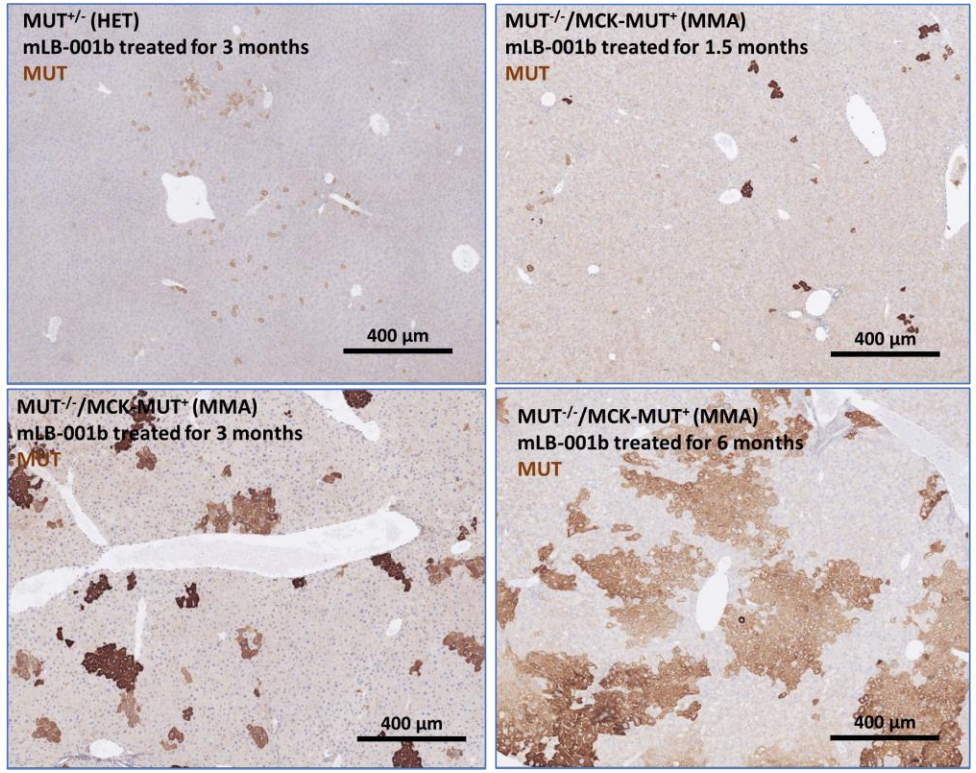
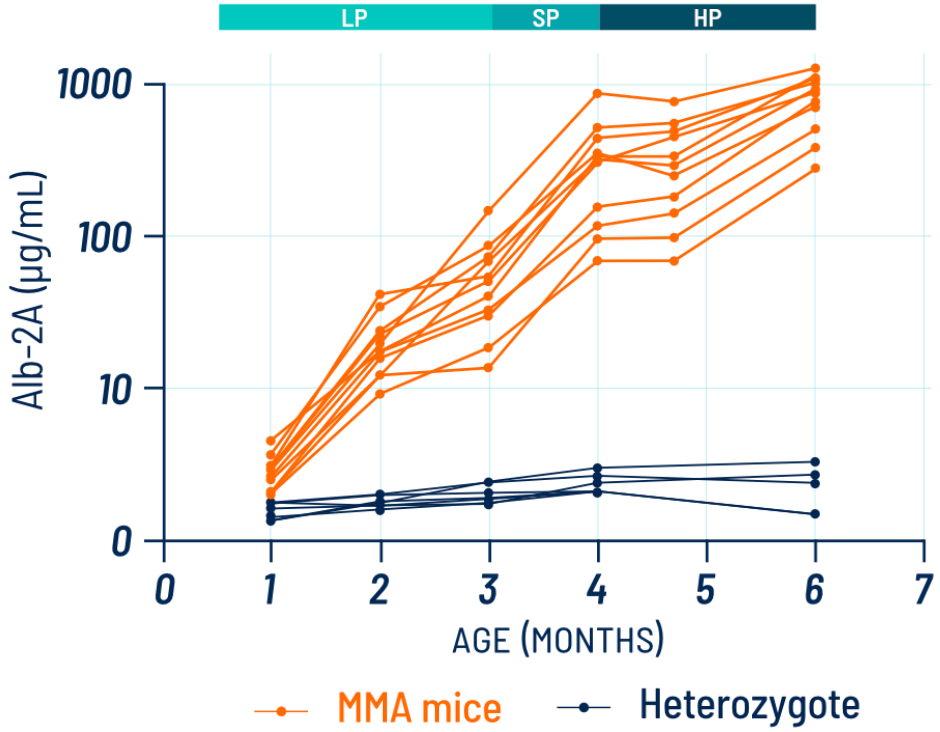
mLB-001 delivers selective advantage to corrected hepatocytes





In diseased MMA mice selective advantage was observed in GeneRide corrected, Mmut expressing hepatocytes, which expanded over time leading to increase levels of circulating biomarker ALB-2A

Ko et al., *ASGCT,* 2020.
Derived from Drouin et al., *ASGCT,* 2020.

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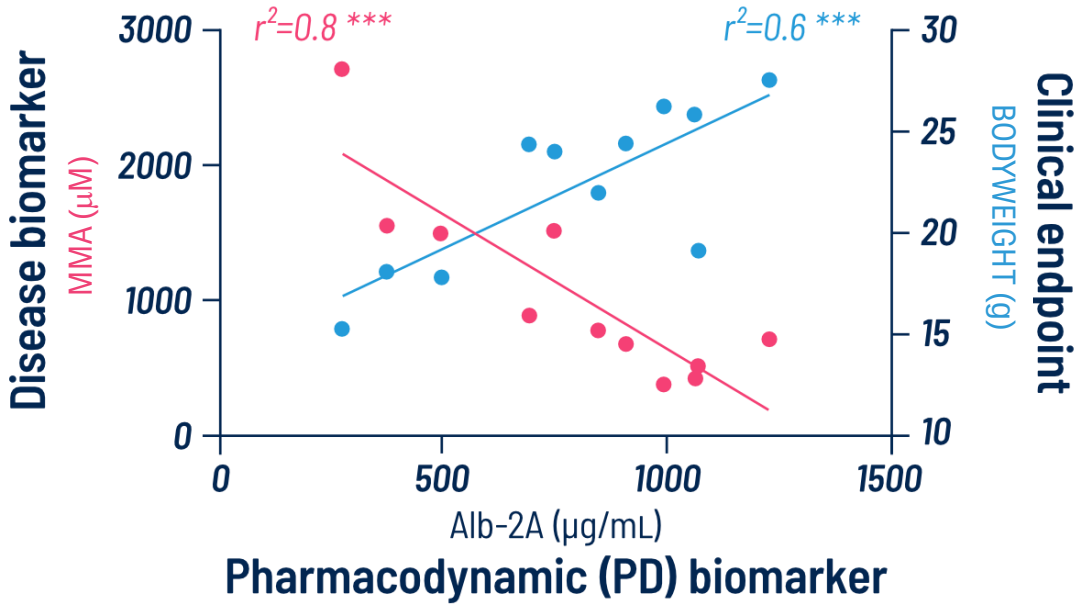
Expansion of GeneRide corrected hepatocytes reveals correlation between PD, disease biomarker, clinical endpoint



Increased PD biomarker correlated with reduction of disease biomarker and improvement in clinically relevant endpoint

Derived from Drouin et al., *ASGCT*, 2020.

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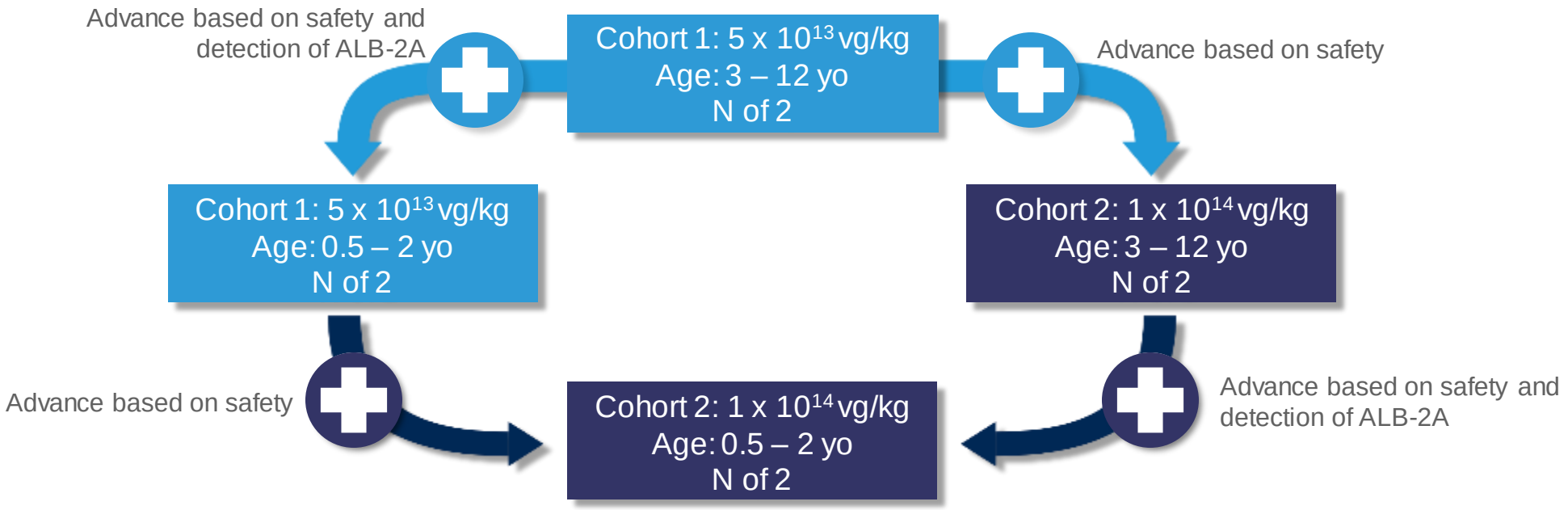
SUNRISE trial design

Open-label, phase 1/2 trial of LB-001 in pediatric MMA patients

sunrise phase 1/2 trial

- One-time treatment, 52-week trial, followed by roll-over to long-term follow-up trial
- 8 patients across 7 investigations sites
- Two cohorts planned with parallel dose escalation and intracohort age de-escalation



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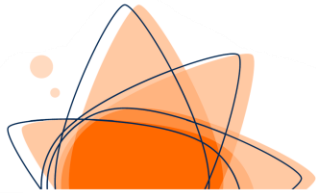
SUNRISE trial design

Safety and preliminary study targeting the most vulnerable patients



sunrise
phase 1/2 trial

- Prophylactic corticosteroid regimen to mitigate potential cellular immune responses
- 6-week staggering interval between each patient
- Primary objective: Assess the safety and tolerability of LB-001
- Secondary objectives: Assess change from baseline in disease biomarkers
- Exploratory objectives: Assess clinical efficacy outcomes

Fulsome catalyst calendar for LB-001

Anticipated milestones and guidance

Fast Track, Rare Pediatric Disease and Orphan Drug designations received in 2020

- **Mid-year 2021** – Enrollment of first patient in Phase 1/2 SUNRISE trial
- **Late 2021** – Operational update from enrollment of additional patients, including dose escalation and age de-escalation
- **Year-end 2021** – SUNRISE trial interim data

GeneRide Platform
LB-301: Preclinical Stage
Pediatric Patients with CN

Takeda

Joint development

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Crigler-Najjar Syndrome (CN)

Joint development

Life-threatening inborn error of metabolism with no treatment options

Incidence:

- 1 in 1,000,000 births (Global)

Prevalence:

- 400 – 1,200 (Global)
- 100 – 300 (US)

Hyperbilirubinemia caused by mutations in *UGT1A1* gene

Results in reduction or lack of bilirubin uridine diphosphate glucoronosyl transferase enzyme leading to toxic accumulation of conjugated bilirubin

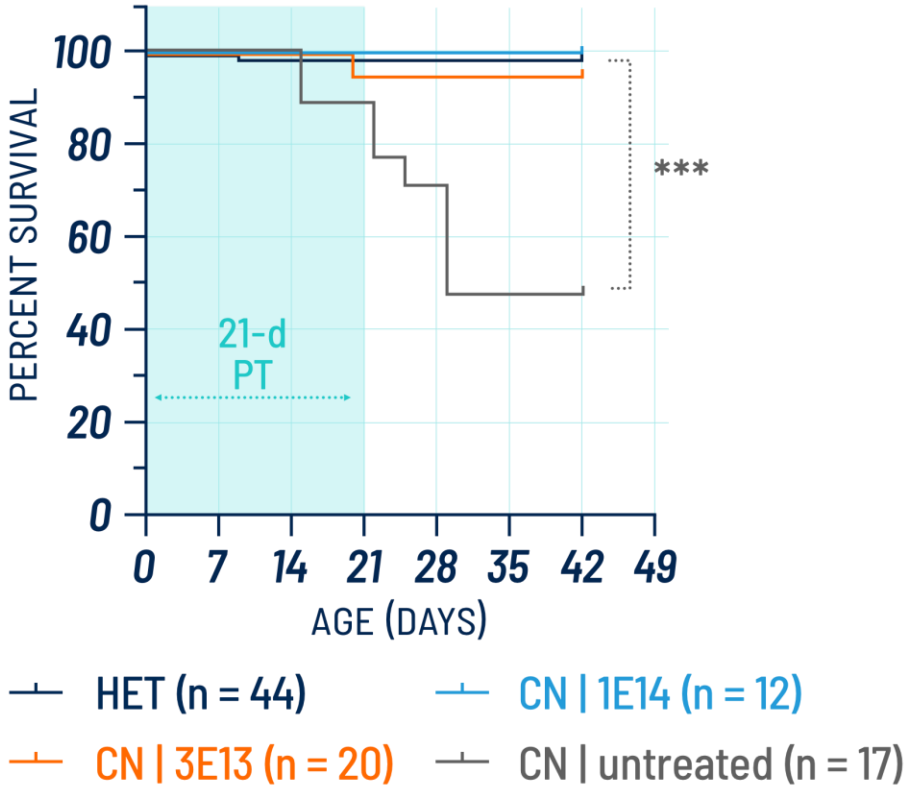
Standard of Care and Outlook:

- Aggressive phototherapy (~12h/day) is only form of management and becomes less effective with age
- No therapeutics, only aggressive management
- High risk of mental impairment, life expectancy of 20 – 30 years
- Liver transplants often needed

Image: SWNS

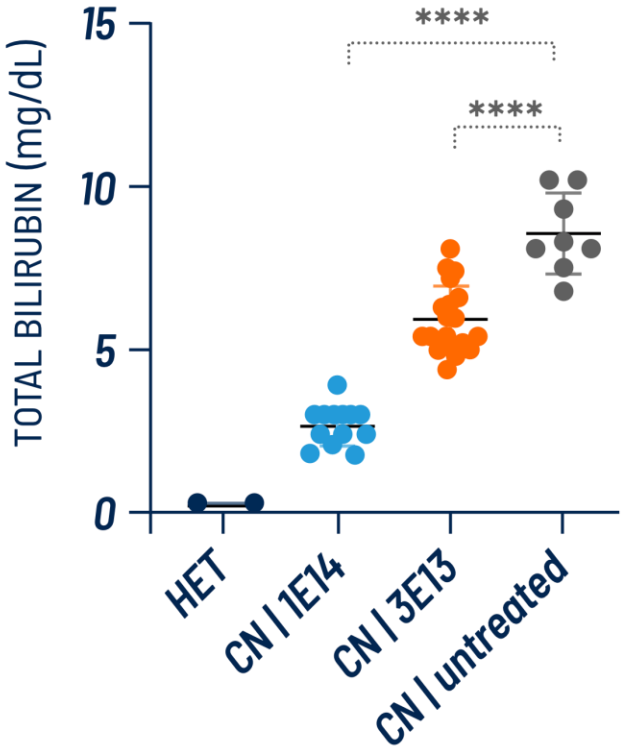
GeneRide™ rescued neonatal Crigler-Najjar mice and reduced clinically relevant circulating biomarker

Survival Rate



*** *p<0.001*

Total Bilirubin



**** *p<0.0001*

Ko et al., *ASGCT*, 2020.

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sAAVy Platform

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Natural AAVs show variable potency across species

LogicBio next generation capsids developed to target human hepatocytes

With AAV5- and AAV8-based DCs, a loss of potency is observed when translating to Humans

Sponsor	DC	Transgene	Capsid Serotype	Mouse		NHP		Human	
				Dose (vg/kg)	Peak expression levels	Dose (vg/kg)	Peak expression levels	Dose (vg/kg)	Peak expression levels
UCL/ SJCRH	n.a.	FIX-WT	AAV8	2×10^{12}	3,000%	2×10^{12}	20-400%	2×10^{12}	5%
			AAV5	2×10^{12}	300%	1×10^{12}	10-30%	n.a.	n.a.
uniQure	AMT-060	FIX-WT	AAV5	n.a.	n.a.	5×10^{12}	15%	2×10^{13}	6%
Biomarin	BMN 270	BDD-FVIII	AAV5	2×10^{13}	80%	3.6×10^{13}	40%	6×10^{13}	20%
Spark	SPK-8011	BDD-FVIII	LK03	n.a.	n.a.	2×10^{12}	20%	1×10^{12}	15%

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Developing capsids for highly effective gene therapy products

Therapeutic Level

EXPRESSION

Low dose:

10^{12} vg/kg

commonly accepted sustainable dose for liver disease patients in clinical trials

Low COGS per patient

(estimation)

< $10K

Specific Tissue Tropism

Ensure a targeted delivery of the payload

High Potency

Potency is a product of capsid transduction and GoI expression

Address Immunogenicity

Limit immune response & seroprevalence

Manufacturability

Cost-effective high-yield manufacturing process

A 3-step platform enhancing AAV's key properties

Enhanced Properties:

1 **Novel AAV Design:**

2 **Selection of novel AAV:**

3 **Process Development:**

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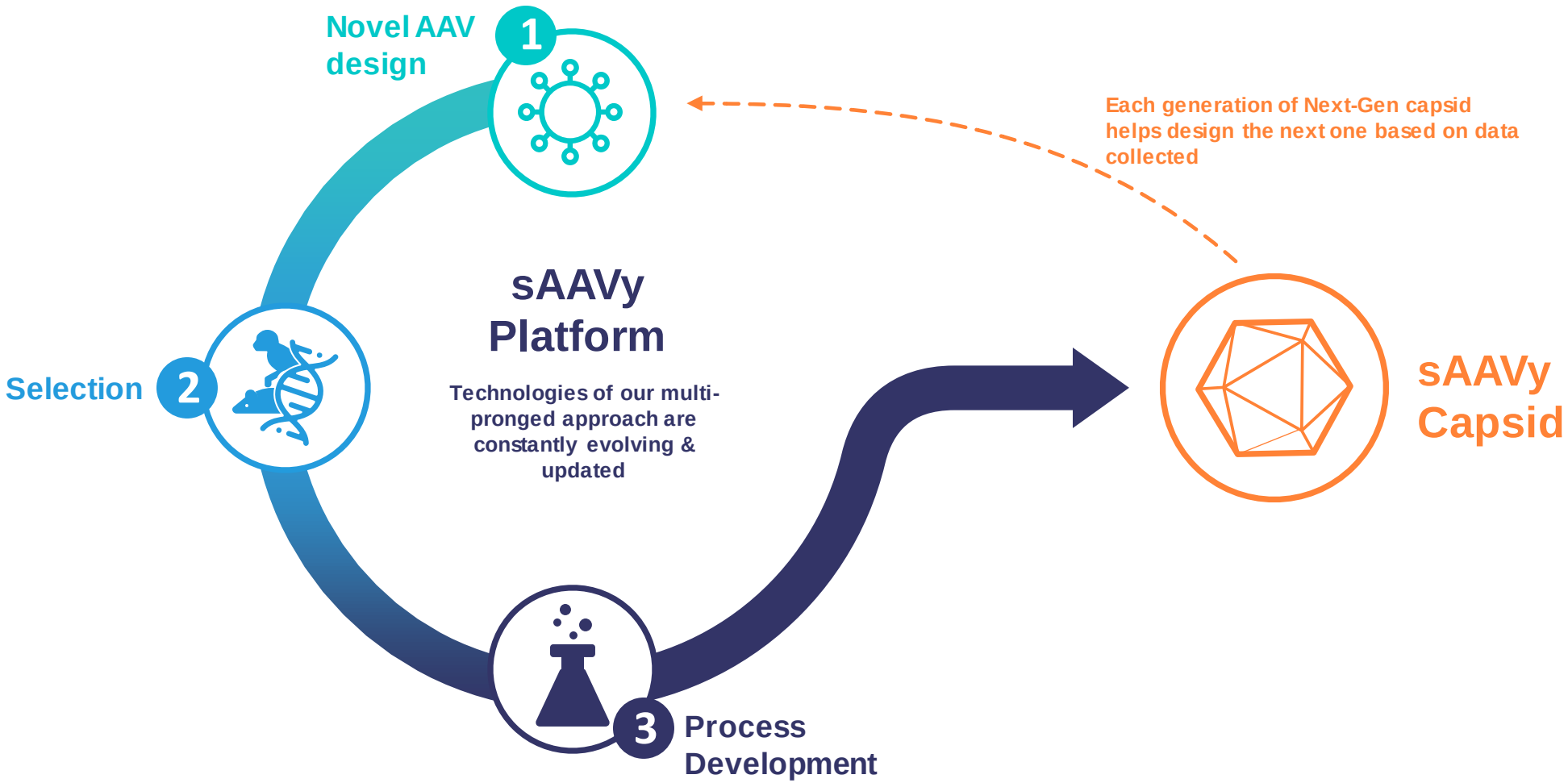
An evolutive and iterative ‘tech-sAAVy’ development platform



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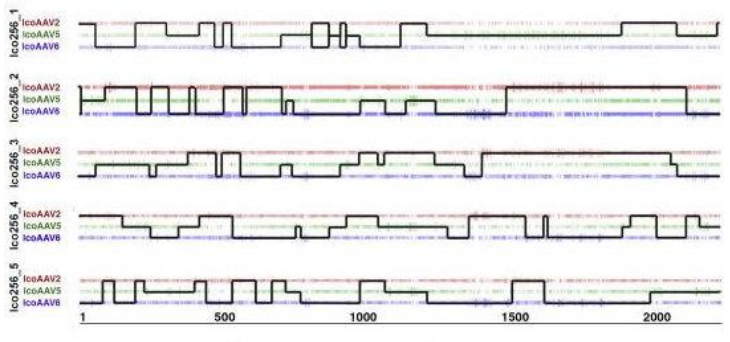
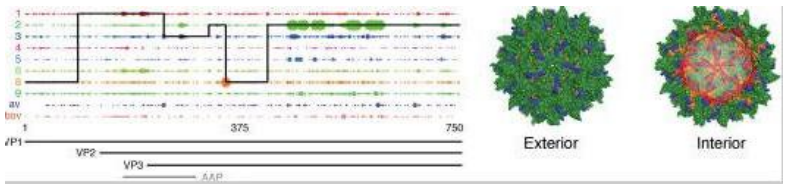
Designing massive and highly variable AAV libraries with CMRI state-of-the-art bioengineering technologies

1

Novel AAV design



Cabanes et al (2018)



Paulk NK et al (2018)

DIRECTED EVOLUTION

Library creation using:

- *In silico* design
- Machine learning
- Enhanced DNA shuffling enhanced through sequence optimization
- EP-PCR mutagenesis
- Peptide library display

Selection Screening with clinically predictive models

RATIONALE DESIGN

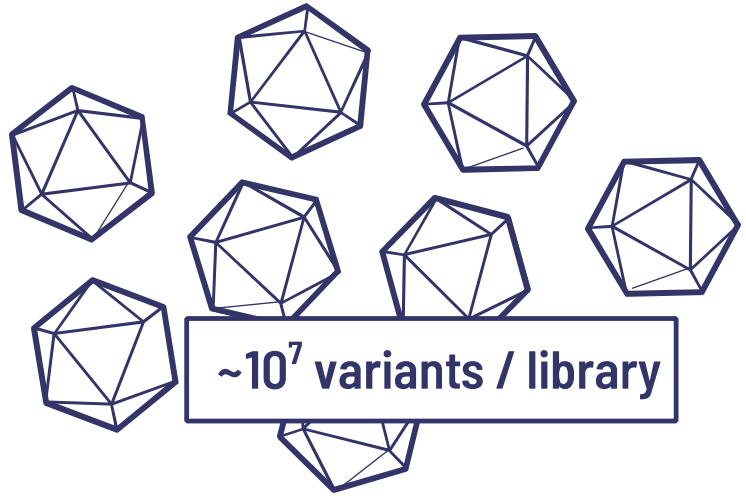
Directed Mutagenesis

Sequence analysis

Next Generation Sequencing (NGS)

Amino acid sequence and structural composition mapping

DISCOVERY OF NATURAL AAV VARIANTS



Highly variable AAV libraries

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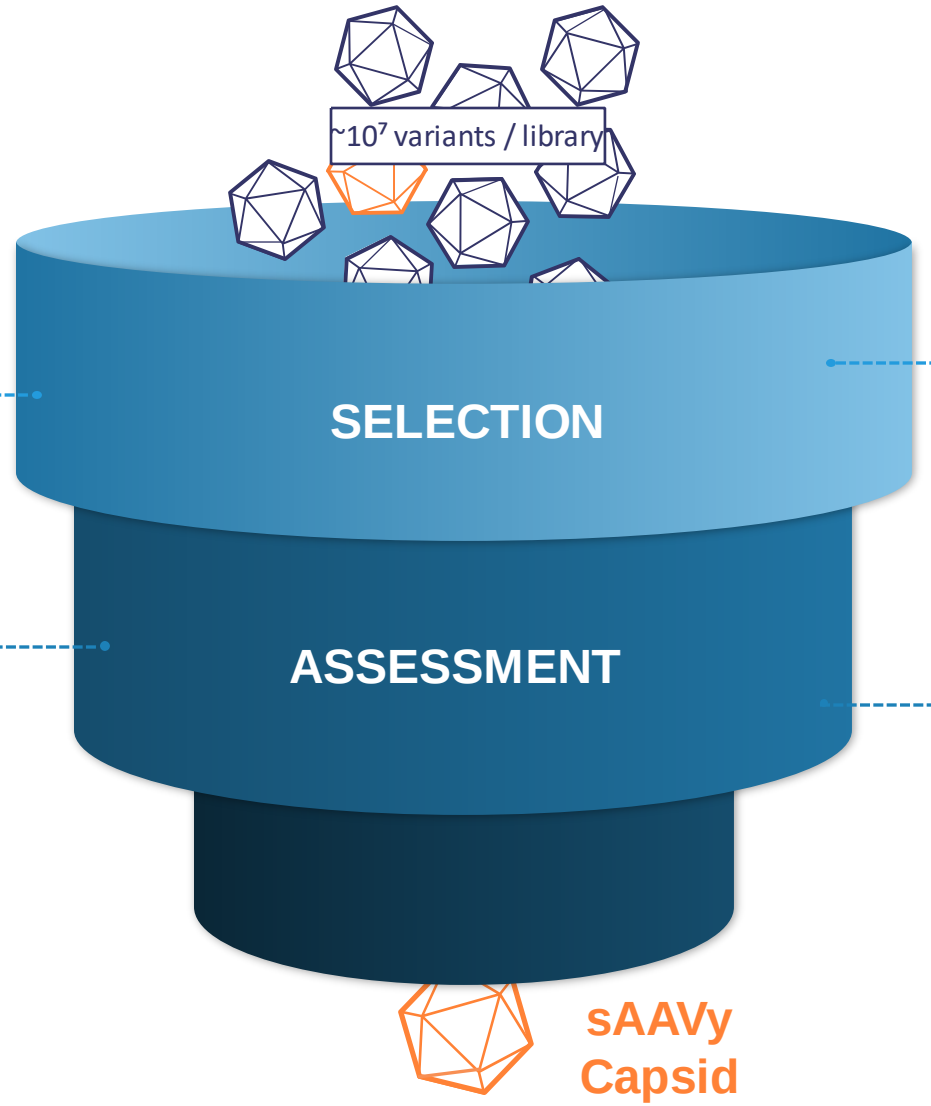
AAV selection & assessment in clinically predictive models

2 **Selection**

Multiple rounds of selection in xenograft humanized mice and human perfused tissues*

Confirmatory studies for best candidates.



Tissue Tropism
- Selective pressure with tissue relevant models

Manufacturability
- Screening for high yields

Functional Expression
- Next Generation Sequencing
- Confirmatory studies in NHP

Low Immunogenicity
- Enhanced resistance to NAbs
- Seroprevalence studies

* CMRI technology

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Assessing capsid manufacturability through GMP-like process

Process Development

AmBr 250ml Modular

Capsid manufacturing yields assessed in PoC bioreactors scaling down GMP process designed to allow an early COGs projection

Single use STR 50L

Confirmatory assays scaled up to 50L and modeling industrial scales

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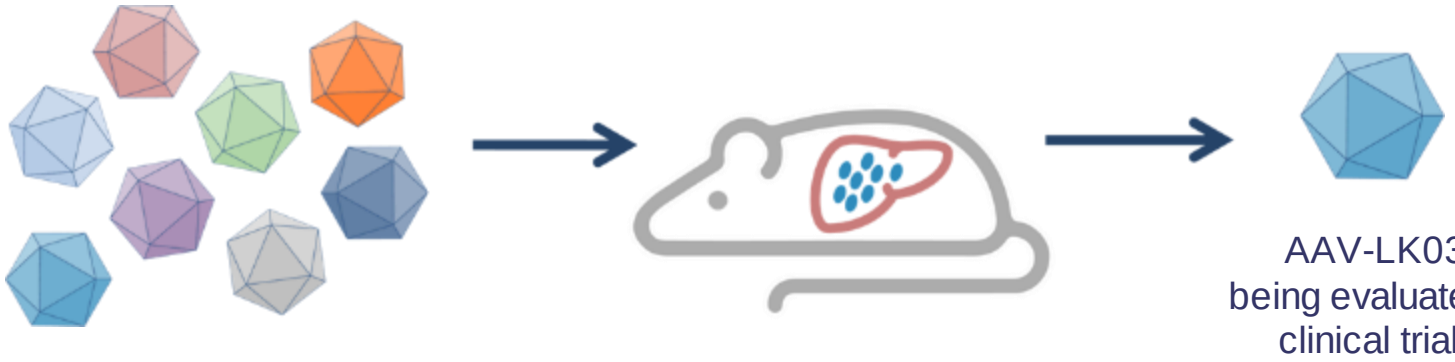
LK03: initial clinical validation

Technologies used to identify LK03 were enhanced in our sAAVy™ discovery platform

- Optimized to target human hepatocytes: ~30x more potent than AAV5 in ongoing Hemophilia A clinical trials[1]
- Preexisting neutralizing antibodies rate of 23% (n=323 human samples) compared to a rate of 19% for AAV8[2]

Lisowski et al., *Nature*, 2014



1. Based on BioMarin's dose of 6e13 vg/kg and Spark Therapeutics' dose of 2e12 vg/kg
2. Perocheau *et al.*, *Hum Gene Ther*, 2018

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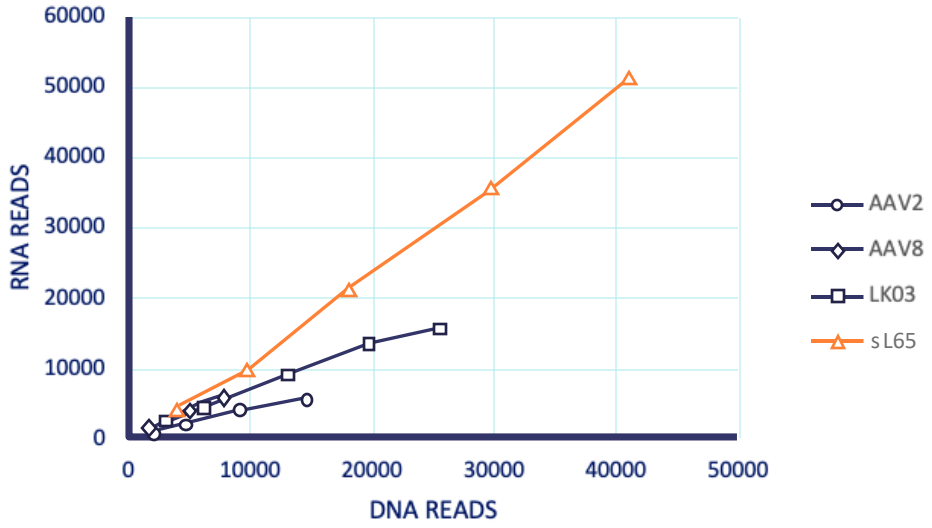
sAAVy platform improves upon the LK03 discovery engine

	Design	Selection	Process Development
LK03	Library creation shuffling sequences of 10 serotypes	Xenografts of humanized mice with low human hepatocyte repopulation In vitro transduction assessment	⊘
sL65	Library creation shuffling sequences of 12 serotypes Enhanced shuffling through sequence optimization Early focus on manufacturability	Xenografts of humanized mice with high human hepatocyte repopulation In vivo transduction assessment with next generation sequencing (NGS) NHP studies	Confirmation of GMP-like compatibility of AAV Improved yield with GMP-like process development

Derived from Cabanes-Creus et al., *ASGCT*, 2020.

sL65 demonstrates improved functional transduction over AAV2, AAV8 and LK03

ENHANCED EXPRESSION OBSERVED WITH sL65



	TRANSDUCTION	EXPRESSION	POTENCY TRANS X EXP
sL65	7.8	1.3	10.4
LK03	5.7	0.8	4.7
AAV2	2.9	0.5	1.5
AAV8	1.0	1.0	1.0

Potency improvement:
10-fold AAV8
2-fold LK03

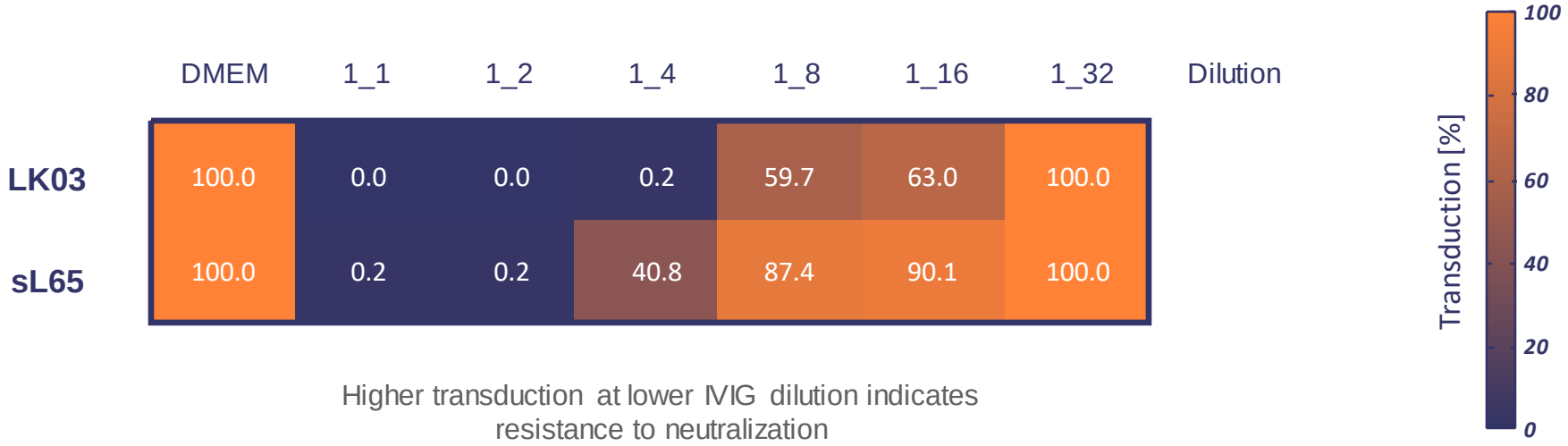
- Xenograft humanized mice are treated with capsids with different barcodes corresponding to different doses
- Plotting RNA (expression) against DNA (transduction) allows for the calculation of expression rates
- A steeper slope indicates a capsid has enhanced functional transduction properties

Derived from Cabanes-Creus et al., *ASGCT*, 2020.

LogicBio THERAPEUTICS

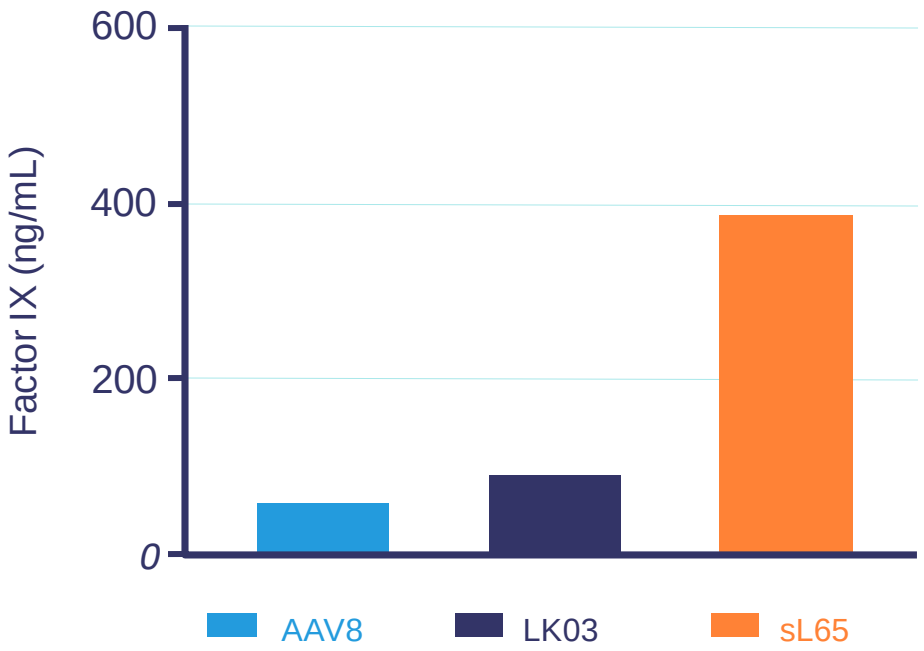
sL65 displays improved immunological profile vs. LK03

- sL65 was tested for IVIG neutralization in HuH-7 cells in vitro
- Transduction efficiency was normalized to no-IVIG control (DMEM)
- sL65 displays less neutralization by IVIG than AAV-LK03



Higher transduction at lower IVIG dilution indicates resistance to neutralization

sL65 : Best performer in NHP with FIX as reporter gene

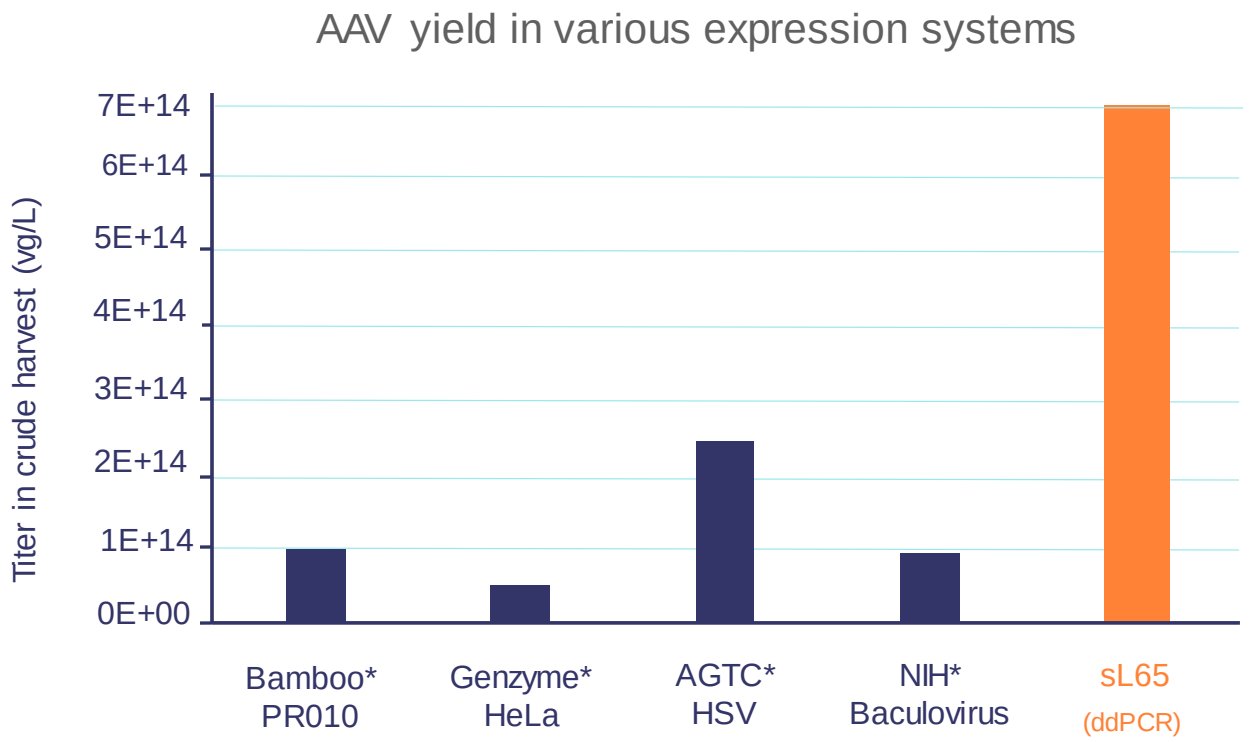


Dose: 3e12 vg/kg

- sL65 was evaluated in NHP with hFIX as a reporter
- Compared to LK03 (the most potent liver-targeted clinical capsid), sL65 encapsidated cassette led to 4x higher level of circulating hFIX
- Complete data package (safety, biodistribution, seroprevalence of neutralizing antibody etc) expected to be disclosed in early 2021

LogicBio THERAPEUTICS

sL65 shows outstanding production yields using LogicBio's proprietary process



** Published data, reviewed by Merten, 2016 – yield assessed by quantitative Polymerase Chain Reaction (qPCR)*

LogicBio THERAPEUTICS

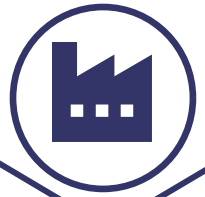
sL65 reaching LogicBio's objective gene therapy TPP

Improved functional transduction of human hepatocytes vs. LK03

Improved immunological profile vs. LK03

Best performer in NHP with FIX as a reporter gene

High manufacturing yields vs. published competition data



Therapeutic Level

EXPRESSION

Low dose:

10^{12} vg/kg

commonly accepted sustainable for patients in clinical trials

< $10K

Low COGS per patient (estimation)

LogicBio THERAPEUTICS

Experienced leadership team

Extensive rare disease drug development experience with a strong track record

Fred Chereau
President and CEO

Kyle Chiang, Ph.D.
Chief Operating Officer

Mariana Nacht, Ph.D.
Chief Scientific Officer

Cecilia Jones
Chief Financial Officer

Daniel Gruskin, M.D.
SVP, Head of Clinical Development

Andrea Paul
General Counsel and Corporate Secretary

Matthias Hebben, Ph.D.
Global VP, Head of Technology Development

Carol Sherako
VP, Program Management

Marie Payton
VP, Clinical Operations

Peter Pechan
VP, Gene Therapy

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Padlock Therapeutics · Peptimmune · Pervasis · The Rockefeller University · Solid Biosciences · The Scripps Research Institute · Shire · valneva · Verastem · Voyager Therapeutics

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RIDE

smart · fast · together ·

FOR PATIENTS